ORAL PRESENTATIONS

Resumen #00003307 en

Effect of maternal sunlight duration and vitamin D on the growth of 2~5-year-old children: a mother-child pair cohort in Shanghai

Effects of Environmental Climate Change on Early Life Health Setting in Future Generations.
Li Cheng (1), Xu Jing-Jing (2), Chen Si-Yue (3), Wu Yan-Ting (4)
(1) Institute of Reproduction and Development, Obstetrics and Gynecology Hospital of Fudan University, (2) Obstetrics and Gynecology Hospital, Institute of Reproduction and Development, Fudan University, (3) Institute of Reproduction and Development, Fudan University, (4) Fudan University

Background/aims:
Vitamin D (VD) deficiency can cause adverse pregnancy outcomes for both mothers and infants. Furthermore, perinatal sunlight exposure has also been proved to reduce adverse outcomes correspondingly. Based on the DOHaD theory, whether sunlight exposure and VD have interactive effect on child growth is not studied.

Methods:
We enrolled 5437 mother-child pairs between 2014 and 2020 in Shanghai, with approval of the ethics committee of Obstetrics and Gynecology Hospital, Fudan University. Maternal VD were tested during the 1st trimester, and sunlight duration were estimated according to the daily report from China National Weather Data Sharing System. The growth of 2~5-year-old offspring were classified according to weight-for-length standard of WHO. The effects of sunlight duration and VD on child growth were evaluated via generalized linear models.

Results:
In particular, maternal exposure to increasing sunlight duration was associated with a reduced risk in overweight and obesity (OWO) during 2~5 years old in offspring, especially during the 1st (aOR=0.749, 95%CI: 0.574-0.978) and 2nd trimester (aOR=0.503, 95%CI: 0.382-0.661). Though maternal exposure to increasing sunlight duration were shown to increase the risk of undergrowth during 3rd trimester (aOR=1.523, 95%CI: 1.064-2.180), it indicated null significance for entire pregnancy (aOR=1.325, 95%CI: 0.673-2.690). Notably, this protective effect of maternal sunlight duration on OWO in offspring were only found in pregnant women with sufficient VD (aOR=0.244, 95%CI: 0.089-0.669), rather than those with VD deficiency (aOR=0.885, 95%CI: 0.430-1.819). Interactive analysis was also indicated that maternal exposure to increasing sunlight duration and reduced VD level had interactive effect in reducing the incidence rate in OWO in offspring (p interactive=0.046).

Conclusions:
In summary, maternal VD status during early pregnancy and sunlight exposure during the entire pregnancy are critical to the growth of 2~5-year-old offspring. Thus, it is urgent for pregnant women supplement VD and increase sunlight exposure to reduce the burden of OWO in their offspring.

Funding:
Young Elite Scientists Sponsorship Program by CAST (YESS20210294), Municipal Human Resources Development Program for Outstanding Young Talents in Medical and Health Sciences in Shanghai (2022YQ016)

Key-words: (up to 5): sunlight duration, vitamin D, overweight and obesity, undergrowth, interactive effect

Resumen #00003455 en

Associations Between Cardiometabolic Profile in Pregnancy and Risk of Primary Dysmenorrhea in Offspring: The ABCD Study

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle, Big Data and Cohorts in DOHaD Research.

Zhou Siyu (1), Shkarpa Nikol (2), Brouwer Cathy (1), van den Boogaard Emmy (3), Twickler Theodorus B. (2), Vrijkotte Tanja G.M. (1)

(1) Department of Public and Occupational Health, Amsterdam University Medical Center, (2) Department of Endocrinology, Diabetology and Metabolism, AZ Monica, (3) Department of Obstetrics and gynaecology, Amsterdam University Medical Center

Background/aims:

Primary dysmenorrhea (PD), characterized by pain during menstruation and associated social consequences, affects the majority of reproductive age women. As several cardiometabolic aspects contribute to the presence of PD, we aim to evaluate whether the fetal programming hypothesis, related to intrauterine conditions affecting offspring's reproductive health later in life, could be applicable. To evaluate to which extent the individual and clustered maternal cardiometabolic profile during pregnancy are associated with dysmenorrhea in female offspring at age 15-16 years, and whether these associations are mediated by the offspring's age at menarche.

Methods:

Data were obtained from a prospective birth cohort, the Amsterdam Born Children and their Development (ABCD) study. Mothers with menstruating female offspring were included (n=982). PD was defined as menstrual abdominal and/or back pain leading to analgetic use. Maternal cardiometabolic profile during pregnancy period included pre-pregnancy body mass index (pre-pBMI), glucose levels, systolic and diastolic blood pressure, triglycerides, and Apolipoprotein A1 at the 12th week of gestation. Ethical approval was obtained, and written informed consent was provided by all participants. Multivariable logistic regression was performed to analyze both individual and clustered cardiometabolic profile components.

Results:

The prevalence of PD in the ABCD cohort was 49.2%. The risk of dysmenorrhea was higher in offspring of mothers with a higher pre-pBMI (OR: 1.15, 95%CI: 1.01-1.30). This association was partially mediated by an earlier age at menarche.

Conclusions:

Our findings indicate that maternal pre-pBMI is associated with the risk of PD in their offspring at the age of 15-16 years. This association is partially mediated by an earlier age at menarche. In order to better understand PD, our observations suggest the need for future research to take into account the early life (prebirth) courses.

Funding:

This work was financially supported by ZonMw Grant (TOP, 40-00812-98-11010).

Key-words: (up to 5):

primary dysmenorrhea; cardiometabolic profile; age at menarche, intrauterine exposure

Resumen #00004503 en

Fetal and infant growth and the cardiovascular stress response in adolescence – A Cardiovascular Magnetic Resonance Imaging study in a pediatric population-based cohort

Big Data and Cohorts in DOHaD Research.

Kamphuis Arwen (1), Hirsch Alexander (1), Roest Arno (2), Rizopoulos Dimitris (1), Budde Ricardo (1), Jaddoe Vincent (1), Gaillard Romy (1)
(1) Erasmus University Medical Center, (2) Leiden University Medical Center

Background/aims:
Abnormal birth weight and infant weight gain are recognized as risk factors for cardiovascular diseases. Underlying mechanisms remain unclear. Exercise testing can detect subtle differences in cardiovascular function, not present at rest. We examined associations of fetal and infant growth with the cardiovascular stress response in adolescence.

Methods:
We examined a subsample of 207 children from a population-based prospective cohort from fetal life onwards. Fetal and infant growth were assessed from 2nd trimester to 2 years. At 16 years, participants performed an isometric handgrip exercise with continuous heart rate and blood pressure monitoring and cardiovascular magnetic resonance imaging (CMR). Participants gave written informed consent, and ethical considerations are satisfied by institutional medical-ethics-committee-approval.

Results:
Children showed a clear peak in heart rate, systolic and diastolic blood pressure during exercise, followed by a decrease below baseline after exercise cessation, before stabilizing. Higher gestational age was associated with lower systolic blood pressure throughout the exercise (differences (95% confidence interval (CI) (mmHg) per SDS increase in gestational age): rest (-2.24 (-4.23 to -0.25), peak exercise (-2.37 (-4.70 to -0.04), recovery (-2.57 (-4.72 to -0.42)), but not with heart rate or CMR outcomes. No consistent associations were present for birth weight or infant growth with the cardiovascular stress response.

Conclusions:
A lower gestational age at birth is associated with an altered response in systolic blood pressure to exercise. Fetal or infant growth are not associated with differences in cardiovascular response to exercise-induced stress in adolescence, in a relatively healthy population. Follow-up of children born preterm is important to enable early identification and prevention of cardiovascular disease development.

Funding:
Netherlands Organization for Health Research and Development, NWO, ZonMw VIDI Grant 09150172110034

Key-words: (up to 5):
cardiovascular stress response, infant growth, fetal growth, birth weight, cardiac MRI

Resumen #00004754 en

Ultra-processed food consumption and cardiovascular health in Canadian children

Big Data and Cohorts in DOHaD Research.

Chen Zheng Hao (1), Mousavi Sara (1), Moraes Theo J (1), Simons Elinor (2), Mandhane Piushkumar J (3), Turvey Stuart E (4), Subbarao Padmaja (1), Miliku Kozeta (1)
(1) University of Toronto, (2) University of Manitoba, (3) University of Alberta, (4) University of British Columbia

Background/aims:
Cardiovascular diseases (CVD) are the leading cause of death, with risk factors like high BMI, body fat and blood pressure tracking from childhood to adulthood. Diet is a key modifiable determinant of CVD risk factors; and in recent decades, nutritionally imbalanced, shelf-stable ultra-processed foods (UPF) have displaced minimally processed foods (MPF) in retail. Given Canada's high UPF consumption, we aimed to examine the association between early-life UPF intake and CVD risk factors and evaluate the potential impact of substituting UPF with MPF.

Methods:
In the CHILD Study (N=1708), UPF and MPF intake at age three years were identified using a food frequency questionnaire and the NOVA classification system. At age eight, BMI z-scores were calculated, fat mass percentage (FM%) was quantified using bioelectrical impedance analysis, and systolic (SBP) and diastolic (DBP) blood pressure were measured using a validated automatic sphygmomanometer. We used linear mixed-effect models and substitution analyses, adjusted for parental and childhood factors. This study was approved by the University of Toronto (REB #47810).

Results:
At age three, average energy intake was 1585 kcal/day, with 45% contributed from UPF. At age eight, average BMI z-score was 0.22, FM% was 19.64%, SBP/DBP were 104/59 mmHg. In the adjusted analyses, every 10% energy intake from UPF was significantly associated with 0.39% (95%CI: 0.04, 0.73) higher FM% and 0.35 mmHg (95%CI: 0.02, 0.69) higher DBP. Substituting 10% of energy contributed from UPF with MPF was associated with 0.50% lower FM% and 0.48 mmHg lower DBP ($p<0.05$). No significant associations were observed for BMI z-scores and SBP.

Conclusions:
Substituting UPF with MPF in early-life may reduce the likelihood of CVD risk factor development. Our findings highlight the role of childhood dietary exposures in informing prevention and intervention strategies to shape long-term cardiovascular health.

Funding:
Canadian Institutes of Health Research

Key-words: (up to 5):
Adiposity, Cardiovascular health, Child diet, Cohort study, Ultra-processed foods

Resumen #00004861 en

The Impact of Bariatric Surgery on Fetal Growth: Evidence of Growth Restriction – the Rotterdam Periconception Cohort

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Schoenmakers Sam (1), Snoek Katinka (1), Willemsen Sten (1), Felix Janine (1), Laven Joop (1), Steegers-Theunissen Regine (1)
(1) Erasmus MC University Medical Center

Background/aims:
The rising prevalence of bariatric surgery among women of reproductive age is increasingly affecting maternal and fetal health. Our prospective study aims to evaluate the impact of preconception bariatric surgery on embryonic & fetal growth trajectories and birth weight.

Methods:
Women aged 18–45 years with a singleton pregnancy following bariatric surgery were prospectively enrolled in the BEYOND study, embedded in the Rotterdam Periconception Cohort (Predict study), a tertiary hospital-based cohort in the Netherlands. As controls, pregnancies without prior bariatric surgery were prospectively included from the Predict study and, to enhance generalisability, the Generation R Study, a population-based prospective cohort. Growth trajectories of 3D-measured crown-rump length (CRL) and embryonic volume (EV) in the 1st trimester, and fetal biometry in the 2nd and 3rd trimesters, were assessed. Linear mixed models accounted for repeated measures, and logistic regression was applied to evaluate differences in birth weight. All conditions for submission have been satisfied and human welfare and ethical considerations have been met.

Results:
A total of 9,649 pregnancies were included: 91 post-bariatric pregnancies from BEYOND, 1,492 non-bariatric pregnancies from Predict, and 8,066 non-bariatric pregnancies from Generation R. After adjusting for covariates, bariatric surgery was not associated with differences in CRL or EV trajectories. However, both estimated fetal weight and femur length growth rates were reduced in post-bariatric pregnancies compared to controls from 20 weeks gestation onward. Adjusted birth weight was significantly lower in the BEYOND cohort: –258 grams (95% CI: –515 to –2; $p = 0.048$) versus Predict, and –470 grams (95% CI: –709 to –231; $p < 0.001$) versus Generation R.

Conclusions:
Preconception bariatric surgery is not linked to early embryonic growth but is associated with fetal growth restriction from mid-gestation. This pattern suggests a potentially iatrogenic form of fetal growth restriction, possibly related to chronic maternal undernutrition.

Funding:

Key-words: (up to 5):
Bariatric surgery, embryonic growth, fetal growth restriction, birth weight

Resumen #00003446 en

Maternal High-Fat Diet Causes Offspring Hyperresponsiveness Via Insulin Effects on Airway Nerves

Interventional strategies to prevent late-life outcomes resulting from early-life insults, Mechanisms Determining Transgenerational Effects of Health and Disease, Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Williams Kayla R. (1), Fryer Allison D. (1), Jacoby David B. (1), Nie Zhenying (1) (1) Pulmonary and Critical Care Medicine, Oregon Health and Science University

Background/aims:
Children of obese mothers are at higher risk of asthma. Our previous studies showed that offspring of obese mice develop obesity and hyperinsulinemia, which increases airway nerve-mediated bronchoconstriction. Given that neurons innervating the airway express advillin, we tested whether selectively deleting insulin receptors in advillin-expressing neurons prevents airway hyperresponsiveness in offspring of obese dams.

Methods:
Advillin-Cre-ERT2 mice were crossed with floxed insulin receptor mice to create advillin insulin receptor knockout (AIRKO) mice. Six-week-old female AIRKO mice were fed a 45% high-fat diet or 14% regular diet from 8 weeks before breeding until the end of lactation. After weaning, offspring were fed a regular diet. At 8 weeks, some mice were treated with tamoxifen (75mg/kg, i.p. for 5 days) to deplete insulin receptors, verified by qPCR and RNA basecope. At 16 weeks, bronchoconstriction in response to inhaled 5-hydroxytryptamine (5-HT, 1-100mM) was measured before and after vagotomy. Tracheas were collected and nerves were identified by immunostaining with PGP9.5 antibody, and imaged in 3D using confocal microscopy and IMARIS software.

Results:
Dams on a high fat diet had increased body fat and their offspring exhibited elevated fasting insulin, glucose, and insulin resistance at 16 weeks compared to offspring of regular diet dams. Offspring of obese dams had increased bronchoconstriction to inhaled 5-HT. This hyperresponsiveness was blocked by bilateral vagotomy, confirming it was mediated by airway nerves. Offspring of dams on a high fat diet had increased airway sensory innervation in airway epithelium. Blocking insulin receptors in advillin-positive neurons did not reverse sensory nerve hyperinnervation, but did prevent airway hyperresponsiveness.

Conclusions:
Deleting insulin receptors in advillin-expressing neurons prevents hyperresponsiveness in offspring of obese dams, offering a mechanism to prevent asthma in children of obese mothers.

Funding:
NIH HL164474, NIH HL163087, Jax Pilot grant, NIH S10OD034444, NHLBI HL131525, NIH T32GM142619-01 and T32-5T32HL083808-14.

Key-words: (up to 5):
Insulin, Airway Hyperresponsiveness, Maternal High-Fat Diet

Resumen #00004492 en

The effect of prenatal exercise mode on infant cardiometabolic risk

Interventional strategies to prevent late-life outcomes resulting from early-life insults

May Linda (1), Roenker Brittany (1), Kern Kara (2), Steen Dylan (1), Wisseman Breanna (3), DeVente James (1),
Mouro Steven (1), Rossa Lindsey (1), Ollmann Caitlyn (1)
(1) East Carolina University, (2) Gannon University, (3) University of Rhode Island

Background/aims:
DOHaD supports that gestational obesity leads to an increased risk to offspring of future obesity and cardiometabolic disease. Accumulating evidence suggests the importance of the intrauterine environment on offspring cardiometabolic profiles. Although aerobic exercise during pregnancy is well-established as safe and effective for both mother and infant, it is unknown which mode of prenatal exercise provides the greatest benefit for offspring health, specifically decreased cardiometabolic risk (CMR). The purpose of this study is to examine the effects of exercise modes during pregnancy on 1-month infant CMR.

Methods:
Pregnant women were recruited and randomized to aerobic (AE), resistance (RE), combination (CE), or control (CON) groups. Participants completed 150 min/week of supervised exercise. After delivery, 1-month infant CMR was assessed using a standardized sum of z-scores of low-density lipoproteins (LDL), inverse high-density lipoprotein (HDL), abdominal circumference (AC), and body mass index (BMI). ANOVAs were used to compare differences between groups; data was stratified by pre-pregnancy BMI (healthy weight vs. Overweight-obese) and infant sex. Regressions assessed predictors of 1-month CMR. Correlations assessed the relationship between 1-month CMR and pre-pregnancy BMI with potential confounding variables.

Results:
Groups were similar in maternal, birth, and 1-month descriptors. Trends for decreased CMR included: any mode of prenatal exercise (p=.08), relative to controls; in infants of healthy weight women (HW) (p=.15), but not infants of overweight-obese (OO) women; and in female (F) (p=.13) and male (M) (p=.23) infants. Although there is a positive correlation between 1-month infant CMR and pre-pregnancy BMI (p=0.048), this relationship is reversed with AE, increased weekly intensity, weekly frequency, weekly duration, total training, and total intensity.

Conclusions:
Maternal exercise mode as well as increased weekly frequency, duration, and intensity decreased 1-month infant CMR. Further research is needed to more clearly understand the most efficient exercise prescription during pregnancy to decrease offspring CMR.

Funding:
American Heart Association #18IPA34150006 and National Institutes of Health #R01DK137945

Key-words: (up to 5):
pregnancy, exercise, mode, infant, cardiometabolic

Resumen #00004719 en

Gestational stress impairs endothelium-dependent vasodilation and redox homeostasis in male and female offspring: the effects of aerobic training

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Monnerat, Juliana (1), Lucchetti, Bianca (1), Teixeira, Gabriel (2), Mentzinger, Juliana (2), Rocha, Luiza (2), Lima, Gabriel (2), Motta, Nadia (2), Rocha, Helena (2), Brito, Fernanda (2), Nóbrega, Antonio Claudio (2), Rocha, Natália (2), Rocha, Gabrielle (1), Medeiros, Renata (1)
(1) Department of Nutrition and Dietetics, Fluminense Federal University, (2) Department of Physiology and Pharmacology, Fluminense Federal University

Background/aims:
Gestational stress can trigger deleterious effects in the adulthood offspring, according to DOHaD concept, and aerobic training may be a strategy to minimize them. The study aimed to evaluate sex-specific responses of aerobic training on vascular parameters in the offspring of Wistar rats submitted to gestational stress.

Methods:
Dams were divided into two groups: control and stress (Ethics Committee n°9518170621), which were submitted to stress protocol from 14th to 21st days of gestation. After birth, the offspring were divided into 3 groups(n=8/group/sex): a) Control(C); b) Stress(S); c) Stress+Training(S+T). Treadmill training was performed 5 days/week, 30 minutes/day for 2 months with maximum effort test (MET) before (60days old) and after (120days old). At 120 days old, body composition (DXA) was performed, blood and thoracic aorta were extracted to determine vascular function and expression of endothelial and antioxidant markers.

Results:
Serum corticosterone was higher in stressed mothers($p=0.04$). Regarding the offspring, MET was higher in S+T(Female $p<0.0001$; Male $p=0.003$). Females submitted to gestational stress presented higher body mass at 60 days old($p=0.0002$), whereas males presented lower body mass at 60($p<0.0001$) and 120 days old($p<0.0001$). Bone mineral content($p<0.0001$) and %body fat was reduced in males($p=0.0488$), whereas %body fat increased in females($p=0.0301$) after stress. Serum superoxide dismutase (SOD) increased in females($p<0.0002$), with no differences in catalase (CAT) and nitrite after stress. Stress impaired acetylcholine-mediated vasodilation and training prevented it(female $p<0.0001$; male $p<0.0001$). Stress reduced expression of eNOS($p=0.0009$), eNOSp($p=0.0076$) and CAT($p=0.0110$) in females, while reduced eNOSp($p=0.05$), GPx($p=0.0180$) and CAT($p=0.0029$) in males.

Conclusions:
Gestational stress impaired endothelium-dependent vasodilation, eNOSp expression and antioxidant response in aorta of the offspring, however, aerobic training was able to minimize these damages.

Funding:
CAPES, FAPERJ.

Key-words: (up to 5):
gestational stress, vascular function, sexual dimorphism.

Resumen #00004873 en

Probiotic Intervention Reduces Maternal Adiposity and Improves Insulin Resistance, Mammary Gland Development, and Milk Composition in Obese Lactating Rats.

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Esparza-Hurtado Natalia (1), Prieto-Ibanez Vidblain (2), Reyes-Castro Luis Antonio (2), Ibañez-Chavez Carlos Alberto (3), Lomas-Soria Consuelo (2), Juarez-Pilares Gimena (4), Zambrano-Gonzalez Elena (3)
(1) Biol Reproducción, Instituto Nacional de Ciencias Médicas y Nutrición SZ/EMCS, Tec de Monterrey, (2) Departamento de Biología de la Reproducción, Instituto Nacional de Ciencias Médicas y Nutrición SZ, (3) Biol Reproducción, Instituto Nacional de Ciencias Médicas y Nutrición SZ/Facultad de Química, UNAM, (4) Depto Investigación Experimental y Bioterio, Instituto Nacional de Ciencias Médicas y Nutrición SZ

Background/aims:
Maternal obesity is associated with intestinal dysbiosis and negatively affects the mother and offspring. The maternal gut microbiome can influence breast milk composition, which in turn affects descendants metabolic programming through its nutrients and bioactive components. Probiotics have the potential to improve maternal microbiota and metabolism, mitigating obesity-associated alterations in the mother and offspring. This study aimed to assess the effects of maternal probiotic supplementation on the mothers' metabolic profile, mammary gland (MG) development and milk composition of obese lactating rats.

Methods:
Female Wistar rats were fed a control (C) or a high fat (MO) diet from weaning. One month before mating, half of each group received a probiotic yeast orally (1×10^{11} CFU/day) until the end of lactation, resulting in four groups: C, CP, MO, and MOP (n=5/group). At 21 days of lactation, maternal body composition and MG development were evaluated. Fasting serum glucose and triglycerides were measured. Milk samples were analyzed for macronutrient content. Insulin and adiponectin levels were determined in serum and milk. Procedures followed institutional ethical guidelines. Statistical analysis by two-way ANOVA ($p<0.05$).

Results:
At 21 days of lactation MO increased adiposity index (AI), serum hormone levels, HOMA-IR, and milk fat and protein content, while reducing mammary gland lobuloalveolar differentiation compared to C. In contrast, MOP showed reduced AI, HOMA-IR, and milk fat content, and improved MG differentiation compared with MO. There is a positive correlation (r2=0.8), between serum and milk insulin concentrations but not for adiponectin. CP and C were comparable across all parameters.

Conclusions:
Maternal probiotic supplementation improved adiposity, insulin resistance, MG development, and milk composition in obese mothers, suggesting a protective effect during lactation and supporting the benefits of this intervention in improving mother and offspring health in maternal obesity.

Funding:
FONCICYT/49/2016

Key-words: (up to 5):
Maternal obesity, Lactation, Intervention, Probiotic, Milk composition

Resumen #00004903 en

Nutritional intervention attenuates links between preconception-pregnancy maternal metabolic factors and placental lipids that impact birthweight and 2-year offspring BMI

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Chan Shiao-Yng (1), Wee Hai Ning (1), Cracknell-Hazra Victoria (2), Yong Hannah (3), Watkins Oliver (1), Cazenave-Gassiot Amaury (4), Bendt Anne (4), Wenk Markus (4), Barton Sheila (5), Lewis Rohan (6), Cutfield Wayne
(7), Godfrey Keith (2)
(1) Department of Obstetrics and Gynaecology, National University of Singapore, (2) NIHR Southampton Biomedical Research Centre, University Hospital Southampton, NHS Foundation Trust, (3) Institute for Human Development and Potential, Agency for Science, Technology and Research, (4) Singapore Lipidomics Incubator, Life Sciences Institute, National University of Singapore, (5) MRC Lifecourse Epidemiology Centre, University of Southampton, (6) Institute of Developmental Sciences, Faculty of Medicine, University of Southampton, (7) Liggins Institute, University of Auckland

Background/aims:
The NiPPeR preconception-pregnancy maternal nutritional intervention RCT reported reduced offspring obesity at 2-years. Maternal lipids transferred to the fetus are regulated extensively by placental lipid metabolism. We hypothesized that maternal metabolic factors at preconception and mid-pregnancy influence placental lipid metabolism, thereby impacting offspring growth, and that these relationships are modifiable by nutritional intervention.

Methods:
Term placentas were collected from 383 NiPPeR trial participants (Singapore, UK, NZ), who were randomized to either control or intervention supplement (myo-inositol, probiotics, enriched micronutrients) starting preconception. Placental lipids (LC-MS-lipidomics) were grouped into 12 WGNCA-clusters. Multiple linear regression examined associations between (1) maternal metabolic factors [BMI, glucose, lipids, HOMA2-IR, Matsuda-index assessed preconception and at 28-weeks' gestation] with placental lipids; (2) placental lipids with birthweight centile and 2-year-offspring-BMI (WHO-z-score), adjusting for key covariates, in stratified control and intervention groups.

Results:
Among controls, the main preconception driver of birthweight was total triglycerides [4.0(95%CI:0.4,7.6)%/SD-factor-increase], while in pregnancy, it was fasting glucose [6.1(2.8,9.5)%/SD]. Both preconception triglycerides [0.18(0.06,0.30)SD/SD-cluster] and 28-week fasting glucose [0.15(0.04,0.27)SD/SD-cluster] associated with a placental lysophospholipid cluster, which partially mediated their effects on birthweight (triglycerides:22%-mediation; glucose:10%-mediation), with placental lysophosphatidyl-ethanolamine-DHA being the main player [4.9%birthweight/SD-LPE-DHA]. Meanwhile, 28-week low-density-lipoprotein was most predictive of 2y-BMI [0.20SD/SD-LDL]. A placental phospholipid-cluster-without-phosphatidylcholines positively associated with 2-year-BMI but no LDL mediation effect was established. The NiPPeR intervention attenuated/reversed these associations.

Conclusions:

Placental lysophospholipids, particularly LPE-DHA, may be key bioactive lipids mediating associations between preconception triglycerides and pregnancy glucose with fetal size. Placental non-phosphatidylcholine phospholipids (bioactive-lipid-precursors, membrane function regulators), may programme offspring in-utero, impacting 2-year-BMI. Nutritional intervention suppression of these associations suggests that preconception-pregnancy supplementation may break links between suboptimal maternal metabolism and dysregulated offspring growth.

Funding:
UK-MRC, SG-NMRC, Gravida-NZ, Nestle-SA

Key-words: (up to 5):
Placenta; lipids; birthweight; pre-conception; nutrition

Resumen #00005410 en

The association of preconceptional and prenatal alcohol exposure with embryonic and fetal growth: insights from the Generation R Next Study

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Rousian Melek (1), Pielage Marin (1), Graafland Naomi (1), Hillegers Manon (2), Steegers Eric (1), El Marroun Hanan (2)

(1) Department of Obstetrics and Gynecology, Erasmus MC, University Medical Center, (2) Department of Child and Adolescent Psychiatry/Psychology, Erasmus MC, University Medical Center

Background/aims:

Prenatal alcohol exposure (PAE) is known to impact development during pregnancy. However, the relationship between low-to-moderate alcohol consumption and embryonic and fetal growth, particularly during the critical first trimester of pregnancy, remains unclear. This study aims to investigate the association between maternal alcohol consumption during the preconception period and pregnancy, and embryonic and fetal growth.

Methods:

This study was conducted in the Generation R Next study, a population based cohort in Rotterdam, the Netherlands. Alcohol consumption was assessed with questionnaires preconceptionally, and during the first, second and third trimester of pregnancy. We investigated preconception and pregnancy alcohol consumption, as well as the frequency of alcohol consumption in these exposure periods. Embryonic and fetal growth was investigated longitudinally using two-dimensional (2D) and three-dimensional (3D) ultrasound datasets conducted at 7, 9, 11-13 and 30 weeks gestational age (GA). During first-trimester pregnancy, the Crown-rump length (CRL) was measured. At 30 weeks GA biometric measurements were performed (head circumference, biparietal diameter, transcerebellar diameter, abdominal circumference, femur length). Additionally, birth weight was investigated.

Results:

The study population included in the analysis was N=1,357 singleton pregnancies. There was no significant association between low-to-moderate alcohol consumption (=<1 consumption/week) during the preconception period or during pregnancy and embryonic growth (2D and 3D CRL). Additionally, alcohol use was not associated with fetal growth measures at 30 weeks GA, nor with birth weight.

Conclusions:

Our results suggest that low-to-moderate alcohol consumption during preconception and early pregnancy may not have a detectable impact on embryonic or fetal growth in a healthy, low-risk cohort. Further research, including studies with larger sample sizes and consideration of high-risk populations, is needed to better understand the effects of alcohol on fetal development.

Funding:

Our research was supported by 'Stichting Vrienden van Sophia', Sophia Children's Hospital, Rotterdam, the Netherlands, grant number; WAR-20-47.

Key-words: (up to 5):

Embryo, Fetus, Prenatal Alcohol Exposure, Growth

Resumen #00004485 en

Arsenic exposure impairs podocyte development in human kidney organoids

Impact of Early Life Exposures and Environmental Pollutants

Haverfield Jenna (1), Sellami Sihem (1), Shao Yiran (2), Awadalla Philip (2), Mann Koren (3), Ryan Aimee (4), Gupta Indra (4)

(1) Research Institute of the McGill University Health Centre, (2) Ontario Institute for Cancer Research, (3) Department of Pharmacology and Therapeutics, McGill University , (4) Departments of Human Genetics and Pediatrics, McGill University

Background/aims:

Arsenic is a widespread environmental contaminant with millions of people worldwide exposed to levels above the World Health Organization's 10 ppb limit. While exposure to arsenic during adulthood is known to increase kidney disease risk, its impact on early kidney development is unknown. In this study, we aimed to evaluate the impact of arsenic toxicity on nephron patterning in human kidney organoids derived from induced pluripotent stem cells (iPSCs).

Methods:

Using an innovative suspension culture method, we generated ~5,000 human kidney organoids per well, each with ~10 nephron-like tubules. Arsenic exposure began at the iPSC stage and continued through differentiation to intermediate mesoderm and mature kidney organoids, simulating exposure from conception to the end of nephrogenesis. Low-dose arsenic concentrations were used (0, 25 and 50 ppb), mimicking real-life exposures around the world.

Results:

Kidney organoids exposed to 0 and 25 ppb of arsenic during nephrogenesis had normal tubule development, with expression and localisation of nephron markers PODXL and WT1 (podocytes), LTL (proximal tubules) and E-cadherin (distal tubules). In contrast, kidney organoids exposed to 50 ppb of arsenic had a marked reduction in WT1 and PODXL-positive cells, but an increase in LTL and E-cadherin-positive cells, suggesting arsenic affects cell fate decisions and nephron patterning. We also developed a deep-learning tool to extract unbiased morphological features from thousands of brightfield images, and principal component analyses showed that kidney organoids exposed to 50 ppb of arsenic follow a distinct developmental trajectory. Finally, RNA-seq is being performed to assess temporal changes in the expression of key differentiation genes during kidney organoid development to identify the molecular mechanisms by which arsenic disrupts nephron patterning.

Conclusions:

Our study identified that the developing kidney is vulnerable to low levels of arsenic toxicity, impairing the development of podocyte-like cells in human kidney organoids. This work yields insight into the developmental origins of arsenic-related kidney disease.

Funding:

This project is part of the DERIVE (DEvelopmental Research on Interactions between Variants and the Environment) research program and is funded by an anonymous donor through the Montreal Children's Hospital Foundation.

Key-words: (up to 5):

Arsenic, environmental exposures, nephrogenesis, kidney organoids, stem cells.

Resumen #00005603 en

Building the Foundations for Early-Life Exposome Research based on the Chilean CHiESS Framework: preliminary data integration results.

Impact of Early Life Exposures and Environmental Pollutants

Urquidi Cinthya (1), Sepúlveda-Peñaloza Alejandro (1), Matus Patricia (1)
(1) Universidad de los Andes

Background/aims:
The double burden of diseases and the accelerated epidemiological transition in Latin America demand innovative frameworks to understand early-life determinants of noncommunicable diseases. In Chile, we developed the Chilean Exposome-Based System for Ecosystems (CHiESS), a technological and conceptual platform integrating multilevel environmental, clinical, and omics data, grounded in the One Health approach. In this abstract, we present an adaptation of the CHiESS framework for investigating childhood obesity by defining early-life exposure levels and sensitive windows, and integrating environmental and social data to identify vulnerability hotspots across Chile.

Methods:
Using CHiESS, we defined early-life exposure levels across critical developmental windows, operationalized through a nested structure based on the communal administrative division. A secondary analysis was conducted by integrating environmental exposure indicators from national surveys and social determinants data from the Longitudinal Survey of Early Childhood (Encuesta Longitudinal de la Primera Infancia, ELPI). Harmonized indicators were geospatially analyzed to construct cumulative exposure profiles at the communal level.

Results:
The adapted CHiESS conceptual framework for childhood obesity research operationalizes environmental and social exposures across four nested levels—ecosystem, community, population, and individual—centered on the commune as the primary spatial unit. Preliminary results show the successful integration of national environmental (pollutants) and social datasets for a historical cohort of 7,540 mother-child dyads, with children born between 2006 and 2008. This integration enabled the identification and geospatial mapping of vulnerability hotspots for childhood obesity across all Chilean communes. Exposures were mapped according to critical sensitive windows, including prenatal development and early childhood (from birth to 5 years of age). This integration enabled a preliminary identification and geospatial mapping of vulnerability hotspots for childhood obesity across all Chilean communes.

Conclusions:
Our preliminary secondary data integration and the adapted conceptual framework demonstrate the potential of exposome platforms and hotspot-based strategies to advance early-life preventive public health policies.

Funding:
Key-words: (up to 5):
childhood obesity, exposome, early environmental exposures

Resumen #00004782 en

Using Mendelian randomization to examine evidence for the adverse transgenerational effect of grandparental smoking and drinking on the birthweight of their grandchildren in the Norwegian HUNT cohort

Big Data and Cohorts in DOHaD Research.

Musa Hanan (1), Brumpton Ben (2), Evans David (3), Moen Gunn-Helen (4)
(1) Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, (2) HUNT Center for Molecular and Clinical Epidemiology, Department of Public Health and Nursing, NTNU , (3) Institute for Molecular Bioscience, University of Queensland, (4) Institute for Molecular Bioscience, University of Queensland

Background/aims:
Adverse exposures in utero, such as maternal smoking and alcohol consumption are known to have negative impacts on offspring. However, it is hotly contested whether adverse intrauterine exposures also elicit long-term effects that persist across generations.

Methods:
We used Mendelian randomization (MR) across three generations in the Norwegian HUNT study to examine whether grandparental smoking and alcohol consumption had causal effects on grandchildren's birthweight. Grandparental exposures were proxied by an unweighted genetic risk score (GRS) constructed from genetic variants associated with either number of alcoholic drinks per week, smoking initiation, or numbers of cigarettes per day (CPD). Our design leveraged all the advantages of the MR method with its robustness against confounding and reverse causality, plus the opportunity to conduct negative control comparisons involving grandfathers vs grandmothers. More than 14,000 genotyped grandparental-parental trios with grandchild's birthweight were included in the analysis across three generations. As a positive control we performed MR analyses on 6006 grandparental-parental trios with parental birthweight. Additionally, we performed observational analysis to show that the know associations between our exposure and birthweight were present in the HUNT cohort.

Results:
As expected, we found that maternal CPD was observationally associated with decreased offspring birthweight. Interestingly this was also the case for maternal grandmother's (but not the other grandparent's) CPD, smoking initiation and alcoholic drinks per day in the case of grandchild's birthweight. Using MR, we found no strong evidence for a causal effect of grandparental alcohol consumption or smoking on grandchild's birthweight. However, grandmaternal GRS for smoking initiation was, as expected, significantly associated with parental birthweight.

Conclusions:
MR provided little evidence for transgenerational effects of smoking and alcohol consumption across three generations, although we cannot rule out small effects.

Funding:
This project is funded by Australian Research Council (Project number: DE220101226) and the Research Council of Norway (Project grant: 325640).

Key-words: (up to 5):
Transgenerational effect, Birthweight, Mendelian Randomization, intrauterine effects, Barker Hypothesis

Resumen #00003426 en

Impact of maternal exposure to ambient air pollution on the risk of live birth defects

Impact of Early Life Exposures and Environmental Pollutants , Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Xu Jing-Jing (1), Chen Wen-Hui (1), Li Tao (2), Wu Yanting (1)
(1) Obstetrics and Gynecology Hospital, Fudan University, (2) International Peace Maternity and Child Health Hospital, Shanghai Jiao Tong University

Background/aims:
Maternal exposure to ambient air pollution has been linked to birth defects. However, the relationship between maternal exposure to each air pollutant and birth defects exhibits significant heterogeneity across different regions and exposure time windows.

Methods:
We enrolled 190372 pregnant women who delivered between 2015 and 2020 at two hospitals in Shanghai. This cohort study was approved by the ethics committee of both hospitals. The effect of perinatal exposure to six critical ambient air pollutants (including PM2.5, PM10, SO2, CO, NO2 and O3) during three different periods (including 3 months before conception, the 1st and 2nd trimester) on the prevalence of different live birth defects were evaluated via generalized linear models.

Results:
We found that an increase in the interquartile range (IQR) of PM2.5 exposure increased the risk of any birth defect (aOR=1.119, 95%CI: 1.051–1.192), including cardiovascular abnormalities (aOR=1.121, 95% CI: 1.005–1.251), orofacial abnormalities (aOR=1.364, 95%CI: 1.063–1.750), urogenital abnormalities (aOR=1.181, 95%CI: 1.028–1.356) and others (aOR=1.265, 95%CI: 1.056–1.515). As the PM10 concentration increased according to the IQR, the risk of orofacial abnormalities increased (aOR =1.447, 95%CI: 1.117–1.875), as did the risk of other abnormalities (aOR=1.225, 95%CI: 1.012–1.483). No associations were found between maternal exposure to SO2, CO, NO2, or O3 and the risk of any birth defects during these 3 periods. Further subgroup analysis stratified by infant sex revealed that pre-conceptional exposure to PM2.5 was associated with the risk of any birth defect (aOR=1.1286, 95%CI: 1.0164–1.2532) for male infants, and for female infants, pre-conceptional exposure to PM10 was associated with an increased risk of orofacial abnormalities (aOR=1.5155, 95%CI: 1.0565–2.1740).

Conclusions:
In summary, our study revealed that maternal exposure to PM2.5 or PM10 during the 3 months before conception increases the risk of birth defects in offspring, with different effects on male and female infants. These findings may have important implications for the development of interventions to reduce the risk of birth defects caused by ambient air pollution.

Funding:
This study was supported by Shanghai Sailing Program (23YF1403600). The authors declare that they have no financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Key-words: (up to 5):
PM2.5; Birth defects; Pre-conceptional exposure; Cohort study

Resumen #00004954 en

Pre-gestational DHA supplementation prevents behavioral impairments in rat offspring exposed to a high-fat diet

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Mercado-Lopez Lorena (1), Carrasco Robinson (2), Muñoz Yasna (1), Beyer María Paz (2), Alvear Ignacio (1), Espinosa Alejandra (1), Dagnino Alexies (2), Valenzuela Rodrigo (1)
(1) Universidad de Chile, (2) Universidad de Valparaíso

Background/aims:
Maternal obesity increases the risk of metabolic disorders and mood disturbances in offspring. N-3 polyunsaturated fatty acids (n-3 PUFAs), particularly docosahexaenoic acid (DHA), are essential for fetal brain development. DHA deficiency has been linked to increased anxiety. Aim: To evaluate the long-term effects of a high-fat diet (HFD) supplemented with 2% DHA on social play, anxiety-like, and depression-like behaviors in Sprague-Dawley rats.

Methods:
Thirty-six Sprague-Dawley female rats were assigned to six dietary groups (n=6 per group): control diet (CD), HFD, CD with 0.1% alpha-linolenic acid (ALA), HFD 0.1% ALA, CD with 2% DHA, and HFD 2% DHA. Diets were administered 12 weeks before mating and continued through gestation and lactation. Behavioral assessments in prepubertal offspring included tests for social play, anxiety-like behavior (elevated plus maze, open field), and depression-like behavior (sucrose preference test). Metabolic and inflammatory markers were measured, and fatty acid composition was analyzed in erythrocytes, adipose tissue, liver, and brain. Two-way ANOVA and Pearson correlation were used for statistical analyses.

Results:
DHA supplementation improved the maternal metabolic profile, increased DHA tissue levels, and reduced the offspring's inflammation. Anxiety-like behavior was significantly reduced in DHA-supplemented dams ($p < 0.05$). Male offspring exposed to HFD or ALA-deficient diets exhibited reduced social play and increased anxiety-like behavior. Anhedonia was observed exclusively in female offspring but was prevented by maternal DHA supplementation. Maternal erythrocyte n-3 PUFA levels negatively correlated with anxiety scores during pregnancy.

Conclusions:
Male offspring were more susceptible to early-life metabolic stress induced by maternal HFD. Maternal DHA supplementation before and during pregnancy exerted protective effects against anxiety-like behaviors in both dams and offspring, emphasizing its relevance for mental health programming during critical developmental windows.

Funding:
This research was supported by FONDECYT Regular 1221098. ANID BECAS/DOCTORADO NACIONAL 21220864.

Key-words: (up to 5):
Docosahexaenoic acid (DHA)
High-fat diet Anxiety-like behavior offspring behavior Pre-gestational diet

Resumen #00006456 en

NGAL Levels in Preterm Children: Associations with Renal Function and Cardiovascular Risk

Role of Infant and Young Child Feeding Practices on Long-Term Health

Suano de Souza Fabiola Isabel (1), Schoeps Denise de Oliveira (2), Holzer-Moraes Simone (2), Hix Sonia (2), Sarni Roseli Oselka Saccardo (2)
(1) Universidade Federal de São Paulo, (2) FMABC

Background/aims:
This study aimed to investigate the association between myeloperoxidase (MPO) and neutrophil gelatinase-associated lipocalin (NGAL) in a cohort of prepubertal preterm children, and to assess alterations in renal function and blood pressure.

Methods:
A cross-sectional study involved 83 prepubertal children, aged 5 to 10 years, including 43 preterm and 30 term-born children. The preterm group had a mean gestational age of 30.3 ± 2.3 weeks and birth weight of 1,150 ± 239 grams. Data collected included perinatal history, current weight, height, and waist circumference, as well as blood pressure (measured three times) and serum levels of creatinine, uric acid, C-reactive protein (CRP), neutrophil gelatinase-associated lipocalin (NGAL), and myeloperoxidase (MPO).
Creatinine and albumin levels were also assessed in a single urine sample.

Results:
No differences were found in markers of renal function, including glomerular filtration rate, NGAL levels and microalbuminuria, between the preterm and term groups. The serum MPO levels were significantly higher in the preterm group (21.1 [14.6–27.1] vs. 8.1 [5.9–13.7] ng/ml; $p < 0.001$). Multiple linear regression analysis identified preterm birth ($\beta = 0.374$; 95% CI: 0.271 to 0.478; $p < 0.001$) and NGAL levels ($\beta = 0.002$; 95% CI: 0.001 to 0.002; $p < 0.001$) as independent predictors of MPO levels. A positive association between NGAL and MPO was observed in the preterm group ($\beta = 1.267$; 95% CI: 0.942 to 1.592; $p < 0.001$), whereas no association was found in the term group ($\beta = –0.004$; 95% CI: –0.251 to 0.242; $p = 0.972$).

Conclusions:
Prematurity was not associated with significant alterations in blood pressure or renal function in prepubertal children. The subclinical inflammation was evident in the preterm group. The association between NGAL and MPO in preterm children suggests that inflammation and tissue damage may contribute to an increased risk of kidney disease in later life, highlighting the importance of long-term monitoring.

Funding:
Fundação de Amparo à Pesquisa do Estado de São Paulo - FAPESP

Key-words: (up to 5):
Cardiovascular risk, renal disease progression, and preterm children.

Resumen #00005421 en

Maternal chronic consumption of different fat sources affects placental gene expression of cellular nutrient transporters in a sex-dependent manner in heterogenic mice

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Alkmim Tulio Cezar Caiafa de (1), de Almeida Jonathas Medeiros (1), Riveros José Andrés Nivia (1), Jorge Erika Cristina (1), de Almeida Fernanda Radicchi Campos Lobato (1)
(1) Universidade Federal de Minas Gerais

Background/aims:
Maternal nutrition plays a crucial role in determining the health status of both mother and offspring. Fat has received considerable attention due to its availability of long-chain polyunsaturated fatty acids (PUFAs), which are critical for placental development. This study aimed to evaluate the effects of the consumption of three widely consumed dietary fats on the placental expression of specific nutrient transporters genes: SNAT1 and SNAT4 (aminoacids), GLUT1 (glucose) and FATP4 (lipids).

Methods:
Nineteen female Swiss mice were randomly allocated to four experimental groups: CC (control; n= 6); SO (soybean oil; n=4); CO (coconut oil; n=4); and LA (lard; n=5). Animals from each experimental group received daily doses of 0.6mL of the respective fat source through gavage (extra 5kcal/day). At E17.5, mice were euthanized for placental samples collection which were grouped in three biological pools per fetal sex and treatment, followed by RNA extraction and gene expression analysis in technical triplicates using quantitative PCR (qPCR) efficiency (approved CEUA/UFMG/Protocol number 103/2020). Data analyses were performed with REST software (QIAGEN, 2009), using a pairwise fixed reallocation randomization test.

Results:
The results revealed sex-specific effects on placental gene expression transporters. In females, SNAT1 expression increased in SO, while SNAT2 and GLUT1 were downregulated in both SO and LA groups($P<0.05$). In contrast, FATP4 expression remained unchanged($P>0.05$). In males, SNAT1 was also upregulated by SO, while SNAT2 expression decreased in SO and LA groups($P<0.05$). GLUT1 expression was upregulated only in males exposed to SO($P<0.05$), suggesting differential glucose transport dynamics compared to females. Notably, FATP4 expression was significantly elevated in males from the CO group($P<0.05$), indicating a potential adaptive response in lipid transport under low-PUFA dietary conditions.

Conclusions:
These findings demonstrate that maternal dietary fat source modulates the expression of placental nutrient transporters in a sex-dependent manner, which may have implications for fetal nutrient supply and long-term metabolic programming.

Funding:
CAPES - Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior

Key-words: (up to 5):

Placenta, cellular nutrient transporters, coconut oil, soybean oil, lard.

Resumen #00005561 en

Sex matters: Disruptions in fetal one-carbon metabolism and placental adaptation

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Castaño-Moreno Erika (1), Carrasco-Negue Karina (2), Díaz de la Garza Rocio (3), Treviño Victor (3), Mujica-Coopman Maria F (4), Yajnik, Chittaranjan S (5), Lamers Yvonne (6), Garmendia Maria L (7), Ronco Ana Maria (8), Casanello Paola (2)

(1) Institute for Obesity Research - Tec de Monterrey, (2) Department of Obstetrics, School of Medicine, Pontificia Universidad Católica de Chile, (3) Institute for Obesity Research, (4) 2Human Nutrition Unit, Institute of Nutrition and Food Technology (INTA), Universidad de Chile, (5) Diabetes Unit, KEM Hospital Research Centre, (6) Food Nutrition and Health Program, Faculty of Land and Food Systems, UBC, (7) Public Nutrition Unit, Institute of Nutrition and Food Technology (INTA), Universidad de Chile, (8) Human Nutrition Unit, Institute of Nutrition and Food Technology (INTA), Universidad de Chile

Background/aims:

Maternal obesity is a known risk factor in the DOHaD framework, influencing offspring health from early development. Fetal sex may modulate responses to maternal nutritional status, but sex-specific effects on placental nutrient transport and neonatal one-carbon metabolism remain underexplored. This study aimed to investigate the interplay between maternal BMI and newborn sex in shaping folate and vitamin B12 pathways at birth.

Methods:

We analyzed 151 newborns stratified by sex and maternal BMI (healthy <25 kg/m² vs. overweight/obesity ≥25 kg/m²). Plasma and red blood cell (RBC) folate forms—5-methyl-THF, 5,10-methenyl-THF, 5-formyl-THF, THF, UMFA, and MeFox—were measured via LC-MS/MS. Vitamin B12 status was evaluated using plasma total B12, holotranscobalamin (holoTC) via ECLIA, and methylmalonic acid (MMA) by LC-MS/MS. Total homocysteine (tHcy) was determined via HPLC/FLD. Placental expression of FOLR1 and TCblR/CD320 was quantified by RT-qPCR and Western blot. Statistical significance was set at $p<0.05$.

Results:

Plasma and RBC concentrations of non-methylated folates (THF, 5-formyl-THF, and 5,10-methenyl-THF) were significantly lower in female neonates. In females, vitamin B12 and holoTC levels were also reduced, with higher MMA levels suggesting a functional B12 deficiency. Interestingly, mothers carrying female fetuses had lower plasma homocysteine levels than those with males. Infants born to women with obesity displayed reduced levels of folate and vitamin B12 markers. Among these, MMA levels were notably higher in female newborns of mothers with obesity. Although the placental expression of folate and B12 transporters was lower in the obesity group, it was higher in female placentas, suggesting a compensatory mechanism.

Conclusions:

Sex-specific differences in neonatal micronutrient status are evident and modulated by maternal obesity. Female newborns appear more susceptible to folate and vitamin B12 insufficiency, with adaptive upregulation of placental transporters potentially mitigating this risk. These findings support the need for maternal BMI and fetal sex-aware nutritional strategies during pregnancy.

Funding:

The present study was funded by the national grants FONDECYT#1171406 & 1221812 (PC), FONDECYT #1150878 (MLG), and FONDECYT #1130188 (AMR). National Doctoral Scholarship ANID (CONICYT) PCHA#21170259 (EC-M), Concurso de Investigación Interdisciplinaria 2018- VRI, Pontificia Universidad Católica de Chile.

Key-words: (up to 5):
Folate metabolism, Vitamin B12, One-carbon metabolism, Maternal obesity, Newborn sex

Resumen #00005683 en

PFAS Mixtures Dysregulate Placental Interferon Signaling: A Link to Infection-Mediated Preterm Birth

Impact of Early Life Exposures and Environmental Pollutants

Yang Zhao (1), Gurdziel Katherine (1), Maxwell Anthony (1), Ding Jiahui (1), Mor Gil (1), Petriello Michael (1) (1) Wayne State University

Background/aims:
Preterm birth(PTB) affects 15 million babies a year globally and is linked to chronic diseases in adulthood. Infection-mediated PTB is associated with ~40% of PTBs, but not all maternal infections elicit PTB. The placenta is a primary mediator of this protection and expresses protective interferons that play a role in placental immune regulation. Downregulation of protective IFNs at the site of the placenta allows for a secondary insult to elicit an uncontrolled inflammatory reaction that would otherwise have been benign. Environmental stressors including viruses and toxicants can inhibit IFN signaling. Per-and poly fluoroalkyl substances (PFAS) are a class of chemicals utilized ubiquitously and have been shown to be immunosuppressive but mechanisms related to PTB are lacking.

Methods:
We exposed human trophoblasts (Swan71) to 3 doses of a mixture of PFOS, PFOA, PFNA, PFHxS, GenX and completed transcriptomics analysis. Differentially expressed genes and enriched pathways were completed for each concentration compared to methanol control. To validate in vitro observations, dams were exposed to the same PFAS mixture from GD8 to 18.5 (2mg/L), and placentas and fetal organs were collected for transcriptomic analysis.

Results:
In human trophoblast cells, we identified 991, 1200, and 6719 genes significantly ($p<0.05$) changed due to PFAS exposure at concentrations of 0.1µM, 1µM, and 10uM, respectively. In the highest concentration, further gene ontology analysis identified 85 biological processes significantly enriched ($q<0.05$), including cellular response to hormone stimulus, cellular response to cytokine stimulus, and embryo development. DEGs included a significant increase in TLR4 (Log2FC:2.04), and significant decreases in IFNAR2 (Log2FC:-0.709) and ISG15(Log2FC:-1.64). In preliminary in vivo analyses, we have observed differences in fetal weight and occipital-frontal diameter due to maternal PFAS.

Conclusions:
Results identified Interferon-related pathways as possible critical mediators of pollutant associated placental toxicity. Future studies will incorporate spatial transcriptomic analyses of mouse placentas to determine the critical role for trophoblasts.

Funding:
This research was supported in part by the National Institute of Environmental Health Sciences [P30ES036084 , R01ES035692-01A1] and the content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Key-words: (up to 5):
PFAS, Placenta, Preterm birth, Infection

Resumen #00004915 en

Geospatial Determinants of Preterm Birth: A Comprehensive GIS Study Across New Zealand

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Salatas Cristal (1), Hobbs Matt (2), Exeter Daniel J (2), Alexander Tanith (2), Wall Clare R (2), Bloomfield Frank H (2) (1) University of Auckland, (2)

Background/aims:
Preterm birth (PTB) is a leading cause of neonatal morbidity and mortality worldwide. While PTB has multifactorial causes, modifiable factors such as nutrition and environmental exposures provide opportunities for intervention. We applied national-level spatiotemporal approaches to identify geographic disparities and risk factors for PTB across New Zealand (NZ), integrating individual-level data with area-level environmental and socioeconomic metrics.

Methods:
National data from 2003 to 2022 (n=1,189,244 births) were obtained from the NZ Integrated Data Infrastructure, a secure virtual environment that links multiple national datasets through individuals' unique national identifiers. We examined these data to determine associations between PTB and socioeconomic characteristics (area-level deprivation deciles: D1=most deprived, income, education), micronutrient supplementation, dietary habits (fruit and vegetable servings), and environmental factors (Healthy Location Index [proximity to food, vape, alcohol, and physical activity outlets] and domicile [urban/rural using StatsNZ 2018 classification]). Multilevel spatial analyses (areas >6 PTBs per population) were conducted. Logistic and multilevel models were applied using RStudio.

Results:
The final analysis included 318,180 births, with 23,705 (7.5%) PTBs. Spatiotemporal analyses revealed persistent PTB hot spots in rural areas, with five clusters identified, four in Counties Manukau and one in Bay of Plenty. Temporal analysis revealed peak cluster intensities in these regions in 2021 and 2010, respectively. Proximity to fast food outlets (OR 1.26, 95% CI: 0.19-1.44) and absence of daily fruit and vegetable servings (OR 1.78, 95% CI: 0.22-2.84) increased odds of PTB. Lower area-level socioeconomic deprivation (OR 1.12 per decile, 95% CI: 1.01-1.24) and tertiary education (OR 1.21, 95% CI: 1-1.46) were also associated with higher odds.

Conclusions:
This novel NZ-based study identifies key risk factors for PTB and highlights the need for geographically tailored interventions, particularly in rural areas and regions with limited access to healthy food options.

Funding:
None

Key-words: (up to 5):
Preterm birth; Geographical Information Systems; Spatial Epidemiology; New Zealand; Preconception

Resumen #00004921 en

Age of Women and Men, Time to Pregnancy and Risk of Miscarriage. The Generation R Next study

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Boxem Aline (1), Blaauwendraad Sophia (1), Mulders Annemarie (1), Bekkers Eline (1), Gaillard Romy (1), Jaddoe Vincent (1)
(1) Erasmus Medical Center

Background/aims:
Older age of women is strongly associated with reduced fertility and early pregnancy complications. It is not known whether these associations are also present across the full range of age, and among both women and men. We assessed the associations of age in women and men with time to pregnancy and miscarriage risk.

Methods:
This population-based prospective cohort study from preconception onwards was conducted in Rotterdam, the Netherlands among 3,604 women and men. Exposures were age at actively pursuing pregnancy and age at conception. Outcomes were fecundability (probability of conceiving within a month); Subfertility (time to pregnancy or duration of actively pursuing pregnancy >12 months or use of assisted reproductive technology); Miscarriage (pregnancy loss <22 weeks of gestation). Ethical considerations are satisfied by institutional medical-ethics-committee-approval.

Results:
As compared to women aged 30-35 years, those aged <25, 25-30 and ≥40 years had increased odds of subfertility (OR 2.14 [95% CI: 1.60, 2.86]; 1.27 [95% CI, 1.06-1.53]; and 2.00 [95% CI, 1.08-3.69], respectively). Similar results were observed for fecundability. As compared to women aged 30-35 years, those aged 35-40 and ≥40 years had strongly increased odds of miscarriage (OR 2.03 [95% CI, 1.52-2.72] and 4.25 [95% CI, 2.54-7.11]). As compared to men aged 30-35 years, those aged <25 years had lower fecundability (Fecundability Ratio (FR) 0.71 [95% CI, 0.58-0.87]. As compared to men aged 30-35 years, those aged ≥40 years had the highest odds of miscarriage (OR, 2.10 [95% CI, 1.43-3.09]).

Conclusions:
Age of both women and men is a strong risk factor for adverse fertility and early pregnancy outcomes. Strategies optimizing age at which couples start family planning will have great individual and public health impact.

Funding:
European Research Council Consolidator Grant (2014-CoG-648916)

Key-words: (up to 5):
Preconception, age, fecundability, subfertility, miscarriage

Resumen #00005459 en

Impact of weight loss on birth weight in obese pregnancies: A real-world analysis

Mechanisms Determining Transgenerational Effects of Health and Disease

Pandya Sunjay (1), Periyathambi Nishanti (2), Patel Vinod (1), Ereneta III Fernando (1), Sukumaran Suganya (1), Sukumar Nithya (2), Weldeselassie Yonas (3), Saravanan Ponnusamy (2)
(1) George Eliot Hospital, (2) University of Warwick , (3) Open University

Background/aims:
Currently, Institute of Medicine (IoM) pregnancy guidelines recommend a 5-9kg weight gain for women with a booking BMI ≥30 for achieving healthy pregnancy outcomes (no caesarean section, appropriate weight for gestational age (AGA) and no-preterm birth). Recent evidence from Sweden and Denmark show weight restriction (<5Kg) in obese pregnancy with gestational diabetes (GDM) can reduce the rates of large for gestational age (LGA). This study aims to investigate the impact of weight restriction and/or weight loss on key birth outcomes in real-world UK multi-ethnic population.

Methods:
A single-centre, observational study involving 1127 consecutive women over a 18-month period. Ethnic specific BMI cut-points (BMI ≥30, South Asian ≥27) were used to define obesity at booking visit. Obese women had routine diet and lifestyle counselling. Based on their total pregnancy weight gain, women were categorised as: weight loss (<0kg), weight restriction (0-4.99kg), IoM recommended weight gain (5-9kg) and excess weight gain (>9kg). A multinomial logistic regression model was used to calculate the adjusted odds ratio (aOR) with IoM recommended weight gain as the reference group. The models were adjusted for key confounders; maternal age, parity, pre-pregnancy BMI, ethnicity, systolic and diastolic blood pressure, and maternal smoking status.

Results:
The 'weight loss' group had significantly lower odds of LGA (aOR 0.32; 95%CI 0.15,0.62) and caesarean section (aOR 0.56; 95%CI 0.33,0.93) compared to the reference group. However, they had higher odds of SGA (aOR 8.03, 95%CI 1.14, 69.9) but had a wide confidence interval. There was no difference in pre-term births.

Conclusions:
In obese pregnancy, weight loss can reduce the risk of LGA and caesarean section rates. However, it may increase the rates of SGA. We recommend that it may be necessary to revise the current IoM recommendations.

Funding:
Nil

Key-words: (up to 5):
Obesity, Weight-gain, Pregnancy, Adverse Outcomes

Resumen #00005800 en

Physical activity patterns across middle childhood and cardiometabolic markers: evidence from the POSGRAD cohort study

Impact of Early Life Exposures and Environmental Pollutants

Henao Morán Santiago Andres (1), Barragán-Vázquez Sofía (2), Fuentes Garcia Ruth Fuentes (3), Vilchis Gil Jenny (4), Ramirez Silva Ivonne (2)
(1) Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, (2) Instituto Nacional de Salud Pública, (3) Universidad Nacional Autonoma de Mexico, (4) Hospital Infantil de Mexico "Federico Gomez"

Background/aims:
Physical activity (PA) is a protective factor for cardiovascular disease but often declines during childhood and adolescence. Longitudinal data on its association with cardiometabolic risk in Latin American children is limited. To examine PA patterns of children from ages 7 to 11 years in the POSGRAD birth cohort and their association with cardiometabolic risk factors (waist circumference, HOMA-IR, triglycerides, total cholesterol, HDL-cholesterol, and LDL-cholesterol) at age 11.

Methods:
A secondary analysis utilized prospective data from 369 children. PA was assessed at ages 7, 9, and 11 through questionnaires, with time and METs calculated for PA, PA trajectories were categorized into five groups based on changes in levels during the visits at ages 7, 9, and 11: 1)decrease, 2)increase, 3)maintenance, 4)increase followed by a decrease, and 5)decrease followed by an increase. Waist circumference and blood samples were collected at age 11. Glucose, insulin, HOMA-IR, triglycerides, total cholesterol, HDL-cholesterol, and LDL-cholesterol were measured. Associations were analyzed using linear regression and quantile regression.

Results:
Compared to a decrease in moderate-vigorous PA METs, maintaining (β= 1.60, IC95% -3.12, 0.08), increasing (β= -1.69, IC95% -3.18, 0.20), or decreasing-increasing-increasing METs (β= -1.44, IC95% -3.08, 0.04) were associated with lower insulin resistance. Maintaining moderate-to-vigorous PA METs (β= -24.11%, IC95% -37.96, -7.42%) and METs of total PA (β= -25.25%, IC95% -39.21, -8.08) were also associated with lower triglyceride concentrations. For HDL-cholesterol, maintaining (β=8.46 %, IC95% 0.42, 17.14%) and increasing time (β=7.92%, IC95% 0.43, 15.96%) and METs (β=9.57 %, IC95% 0.96,
18.91%) in moderate-to-vigorous PA were associated with higher concentrations.

Conclusions:
Our findings indicate that childhood PA impacts cardiometabolic markers in adolescence, including lower insulin resistance and slight effects on HDL cholesterol and triglycerides. This underscores the need to encourage early physical activity, particularly within the Mexican population, due to their significant cardiovascular disease burden.

Funding:
Research was supported by NIH (HD043099, HD058818, HD087606), March of Dimes, Nutricia Foundation, and CONACYT Mexico (87,121, 202,062).

Key-words: (up to 5):
Physical Activity; Cardiometabolic Risk Factors; Longitudinal studies; Lifestyle.

Resumen #00005880 en

Sex-specific effects of cannabidiol on metabolic, immunomodulatory, and redox profile of weaned mice exposed to high-sucrose diet

Impact of Early Life Exposures and Environmental Pollutants

do Carmo Silva Ribeiro Rafael (1), Castro Santos Oliveira Lúcia (1), Marinho Melo Thamys (1), Pessoa Pontes Jaqueline (1), de Fátima Carvalho Brito Camila (1), Marcus de Andrade Paes Antônio (1), Ckless Karina (2), Martins França Lucas (1)

(1) Department of Physiological Sciences, Federal University of Maranhão (UFMA), São Luís, Brazil., (2) Department of Chemistry, SUNY Plattsburgh, United States.

Background/aims:

Excessive consumption of added sugars leads to liver lipid accumulation, insulin resistance, and chronic inflammation, which are key factors for metabolic-associated steatotic liver disease (MASLD) along with low grade inflammation and release of pro-inflammatory cytokines. In this context, cannabidiol (CBD) has emerged as a potential multi-target therapeutic tool. Thus, this study aimed to assess the effects of CBD on metabolic, inflammatory, and redox unbalance induced by early exposure to high-sucrose diet (HSD).

Methods:

Male and female mice were fed either regular chow (10% sucrose; n=7-8/sex) or HSD (25% sucrose) for 13 weeks. After the 10th week, HSD group was split into two subgroups receiving either vehicle (n=7-8/sex) or CBD (10 mg/Kg/day, v.o., n=7-8/sex). Upon treatment completion, overnight fasting mice were anesthetized for blood and tissue collection, which were processed and stored until further analysis (23115.016737/2024-38 CEUA/UFMA).

Results:

CBD effects differed between sexes. In males, treatment did not improve serum markers of metabolic and inflammatory disturbances induced by HSD. Indeed, CBD increased serum triglycerides levels (HSD: 51.62±4.46 vs. HSD-CBD: 70.00±4.29mg/dL, $p<0.05$). On the other hand, in females, CBD treatment restored blood glucose levels (HSD: 145.5±4.69 vs. HSD-CBD: 128.4±5.35 mg/dL, $p<0.05$), mesenteric (HSD: 0,14±0,09 vs. HSD-CBD: 0,12±0.01 g/10g BW, $p<0.05$) and periovarian (HSD: 0.08±0.11 vs. HSD-CBD: 0.04±0.008 g/10g BW, $p<0.01$) adipose tissue accumulation but increased serum IL-1β levels (HSD: 0.35±0.03 vs. HSD-CBD: 0.59±0.07 pg/µg protein, $p<0.05$). Both sexes showed hepatic steatosis, ballooning, and leucocyte infiltration, when exposed to HSD which were partially attenuated only in males upon CBD treatment. In females, CBD treatment led to a reduction in intracellular levels of redox enzymes, including catalase and oxidized peroxiredoxins, compared to the HSD group.

Conclusions:

Our data demonstrate that CBD promotes distinctly opposite effects in males and females, highlighting the critical importance of considering sexual dimorphism in the development of cannabinoid-based therapies.

Funding:

CNPQ; CAPES; FAPEMA

Key-words: (up to 5):

Cannabidiol; Sucrose; Liver Disease; Low grade inflammation

Resumen #00004913 en

Independent and Synergistic Effects of Maternal and Paternal Obesogenic Diets on Adult Outcomes in Sprague-Dawley Rats

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Toor KJ (1), Vickers MH (1), Abbasi M (1), Muralidharan S (1), Ponnampalam AP (2), Firth EC (1), Musson DS (3), Albert BB (1)

(1) Liggins Institute, The University of Auckland, (2) Department of Physiology, The University of Auckland, (3) Department of Nutrition and Dietetics, The University of Auckland

Background/aims:

Independent effects of an obesogenic maternal or paternal diet on offspring outcomes are acknowledged. However, there remains limited data on the effects of combined parental obesity. We investigated the independent and synergistic effects of a parental obesogenic (OB) high-fat:high-sugar diet on outcomes in adult offspring.

Methods:

Male (pat) and female (mat) rats were fed a control diet (CON) or OB diet for five-weeks pre-mating (Animal-EthicsAEC26450). Females continued their diets throughout gestation and lactation. Four groups were established: matCON-patCON, matCON-patOB, matOB-patCON, and matOB-patOB. Offspring were weaned onto a standard chow diet and assessed as adults for body weight, adiposity, and glucose metabolism. Data were analysed using two-way ANOVA.

Results:

Male offspring from matCON-patOB and matOB-patOB groups showed significantly greater post-weaning weight gain compared to matCON-patCON and matOB-patCON ($p<0.001$). Female offspring in all OB groups exhibited increased weight gain relative to matCON-patCON ($p<0.001$). At postnatal day 176, fasting insulin levels and HOMA IR were significantly elevated in males due to patOB ($p<0.05$), while in females both insulin levels and HOMA-IR were increased due to a significant mat×pat interaction ($p<0.05$). Post hoc analysis identified elevated insulin and HOMA-IR in the matOB-patCON group compared to matCON-patCON in females ($p<0.05$). Oral glucose tolerance test derived glucose area under the curve showed no parental effects in either sex. In adult male offspring, patOB was associated with increased total body fat%, fat:lean ratio, and bone mineral content ($p<0.05$), while matOB led to higher bone mineral density ($p<0.05$). patOB increased retroperitoneal fat (%BW) a major visceral fat depot in both sexes ($p<0.05$).

Conclusions:

Maternal and paternal OB diet influenced offspring growth and body composition, with sex-specific effects. patOB showed stronger impact on male offspring, while matOB effects were more prominent in females.

Funding:

Auckland Medical Research Foundation.

Parental diet, Offspring metabolism, Obesity.

Resumen #00004953 en

Folate depletion alters DNA methylation in tissues relevant for childhood leukaemia

Impact of Early Life Exposures and Environmental Pollutants

Saville Jessica (1), Nassar Farah (2), Russell Lisa (3), Padget Kay (4), Cuenin Cyrille (2), Cahais Vincent (2), Ghantous Akram (2), McKay Jill (1)
(1) Northumbria University, (2) International Agency for Research on Cancer, (3) Newcastle University, (4) St George's University

Background/aims:
Epidemiological evidence suggests maternal folate status influences childhood leukaemia risk; however, the underlying mechanisms are unclear. Genetic aberrations, are considered leukaemia-initiating events, however, alone they are not sufficient for disease, with additional 'hits' required. Epigenetic alteration, i.e. DNA methylation, is one mechanism by which maternal folate is likely to contribute to disease. We investigated the relationship between folate depletion and DNA methylation in murine tissues relating to childhood leukaemia.

Methods:
Female mice were allocated low or normal folate diets for 4 weeks before mating and onwards. Offspring were sampled at 17.5 days gestation and weaning. DNA was isolated from fetal livers and bone marrow of weaned mice. Tissues correspond to specific sites of haematopoiesis throughout the lifecycle relevant to leukaemic blasts. Epigenome-wide DNA methylation was profiled using Infinium® MouseMethylation BeadChips. R/Bioconductor packages identified differentially methylated points (DMP) and regions (DMRs).
Pathway analysis was conducted by DAVID.

Results:
There were 598 DMPs (382 hypermethylated/216 hypomethylated) and 363 DMRs with significantly (FDR) altered methylation in response to folate depletion in the fetal liver. In bone marrow, 1206 DMPs (334 hypermethylated/852 hypomethylated) and 565 DMRs had significantly altered methylation in response to folate depletion. Only 3 DMPs and 13 DMRs were altered in both tissue types, suggesting highly tissue specific responses. Pathway analysis suggested 15 and 44 pathways could be altered in response to folate depletion in liver and bone marrow respectively, with 8 overlapping between tissues.

Conclusions:
Whilst loci specific altered methylation appears to be different between tissues, the impact on biological pathways is similar.

Funding:
World Cancer Research Fund UK, as part of the World Cancer Research Fund International grant programme #IIG_FULL_2022_007

Key-words: (up to 5):
Childhood Leukaemia, Maternal Folate Status, DNA Methylation

Resumen #00005006 en

Sex-linked epigenic marks in the rat determine male-female differences in liver metabolism in response to high-calorie feeding and parental obesity

Mechanisms Determining Transgenerational Effects of Health and Disease

Bolaños-Jiménez Francisco (1), García-Santillán Juan Antonio (1), Mezo-González Carla Elena (1), Gourdel Mathilde (2), Croyal Mikaël (2)
(1) Nantes Université, INRAE, UMR 1280, Physiologie des Adaptations Nutritionnelles, Nantes, France., (2) Nantes Université, CHU Nantes, CNRS, INSERM, l'institut du thorax, Nantes, France.

Background/aims:
Maternal or paternal obesity increases the risk in offspring of developing metabolic diseases through a "metabolic programming" process. Like many biological functions, the physiological disturbances resulting from parental obesity vary as a function of sex. However, the molecular mechanisms underlying these gender differences remain largely unknown. This study aimed to determine the role of the epigenetic dichotomy between males and females in the pathological vulnerability induced in offspring by parental obesity.

Methods:
The global liver lipidome profile in male and female control and obese founder rats (F0) and their male and female offspring (F1) was determined by ultra-performance liquid chromatography tandem mass spectrometry, and gene expression and epigenetic analysis were performed, respectively, by real-time PCR and chromatin immunoprecipitation. The experiments were carried out following the principles of laboratory animal care and were approved by the Ethics Committee for Animal Experimentation of the Pays de la Loire region.

Results:
Compared to F0 male rats, female F0 rats exhibited reduced ceramide synthesis and higher levels of the inhibitory epigenetic mark H3K27me3 at the promoter site of the SPT1 gene, which encodes the enzyme that catalyses the first stage of sphingolipid synthesis. These sex differences persisted in obese F0 animals and their offspring. Therefore, high-calorie feeding resulted in an increased concentration of ceramides in the liver of F0 female rats, but not in F0 male rats. Similarly, a higher concentration of ceramides was observed in female, but not male, F1 rats born to obese mothers. Furthermore, paternal, but not maternal, obesity exacerbated the increase in ceramide concentration in response to high-calorie feeding only in F1 female offspring.

Conclusions:
Higher levels of the epigenetic mark H3K27me3 on the SPT1 promoter in female rats determine their differential responses compared to male animals to a high-calorie diet and maternal and paternal obesity.

Funding:
GS-JA and MG-CE were supported by an international Ph.D. fellowship from the Mexican National Council of Science and Technology (CONAHCYT).

Key-words: (up to 5):
Parental obesity, Sex differences, Ceramides, Lipidomics, Epigenetics.

Resumen #00005505 en

Maternal small intestinal maladaptation to high fat diet and viral infection: implications for pregnancy health

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Carvalho Cardoso Lucas (1), Ferraz Thaina (1), Mohammadkhani Sadra (1), Bloise Enrrico (2), Connor Kristin (1) (1) Carleton University, (2) Universidade Federal de Minas Gerais

Background/aims:
Viral infection and obesity adversely impact pregnancy, promoting a pro-inflammatory environment. The gut is the main site for nutrient absorption, however, it is unknown how the maternal small intestine (SI) responds to obesity or infection. We hypothesised that maternal high fat (HF) diet, infection, or their combination, would induce a pro-inflammatory environment, altering intestinal morphology/function, impacting pregnancy and fetal development.

Methods:
Female C57BL/6J mice were exposed to 60% HF or control (CON) diet six weeks before and throughout pregnancy. Pregnant mice were injected with viral mimic Poly(I:C) (POLY) or saline (VEH) 24h before sample collection at gestational day (GD) 12.5, 15.5, 18.5 (n=5-8/group/GD). Circulating levels of pro-inflammatory (IL-5, TNF-α) and anti-inflammatory (IL-10) mediators (Bioplex) and SI Toll-like receptor 3 (Tlr3; pro-inflammatory marker) mRNA levels (qPCR) were quantified. SI morphology (H&E), cell death (immunoreactive (ir)-Caspase3), cell proliferation (ir-Ki67) and fetoplacental weight were measured. Effect of diet and infection were quantified (two-way ANOVA, Tukey's post hoc; $p<0.05$). Ethical considerations were met.

Results:
HF diet alone had no effect on maternal or fetal outcomes. Acute viral infection alone was associated with increased IL-10 and reduced IL-5 levels (GD12.5) in CONPOLY vs. CONVEH, and concomitant higher SI Tlr3 expression (GD12.5;GD18.5). Further, SI surface area was reduced (GD12.5), whilst cell death was increased (GD18.5), in CONPOLY vs. CONVEH, associated with reduced fetal weight (GD18.5). Combined effect of HF diet and infection increased IL-10 and decreased IL-5 levels (GD12.5), and decreased TNF-α levels (GD15.5), and was associated with higher SI Tlr3 expression (GD12.5;GD18.5) in HFPOLY vs. CONVEH. SI surface area was reduced (GD12.5;GD15.5), whilst cell proliferation (GD15.5) and cell death were increased (GD18.5) in HFPOLY vs.CONVEH, associated with reduced fetal weight (GD18.5).

Conclusions:
HF diet and infection induce a local pro-inflammatory environment, compromising intestinal morphology.
This likely contributes to impaired nutrient absorption and fetal growth seen in these pregnancies.

Funding:
Natural Sciences and Engineering Research Council of Canada

Key-words: (up to 5):
maternal health, small intestine, inflammation, obesity

Resumen #00005515 en

Diets with different lipid content during pregnancy and lactation and early-life stress programming the hedonic eating in adolescent rats

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Lena Mariana (1), Peres Ariadni (1), Machado Alessandra (1), Silveira Ana Caroline (1), Trindade Andressa (1), Dalmaz Carla (1), Bast Rachel (1)
(1) Department of Biochemistry, Federal University of Rio Grande do Sul

Background/aims:
Maternal consumption of different lipids during pregnancy and exposure to maternal separation (MS) may program behavioral and metabolic outcomes in offspring, especially during adolescence. Olive oil (OO) could prevent these consequences due to its bioactive compounds. This study evaluated the effects of soybean oil (SO) or OO consumption during gestation/lactation on the feeding behavior of adolescent rats exposed to MS.

Methods:
Pregnant Wistar rats received SO- or OO-enriched diets (CEUA-UFRGS: 37803). Offspring were divided into four groups: (1) non-handled (NH) + SO, (2) NH+OO, (3) MS+SO, and (4) MS+OO. MS occurred from postnatal day (PND) 1–10 (3 h/day). At weaning, rats received standard chow and were submitted to behavioral tests involving palatable food consumption in adolescence. Nucleus accumbens (NAc) and ventral tegmental area (VTA) were collected for Western blotting analysis.

Results:
Food consumption increased over time ($p<0.001$). MS females showed increased body weight ($p=0.009$) and adrenal gland weight ($p<0.001$). In the palatable food search task, maternal OO groups had a longer latency to eat ($p=0.037$). MS+OO rats showed longer latency to eat ($p=0.001$) and increased food intake ($p=0.04$). In the home cage, MS groups consumed more palatable foods ($p=0.029$). MS reduced dopamine D2 receptor immunocontent in the NAc, but OO prevented this effect ($p=0.042$). MS females also showed reduced immunocontent of CRHR1 in the VTA, with OO preventing this reduction ($p=0.028$). Opposite effects were observed in MS+OO males ($p=0.042$).

Conclusions:
MS led to dysfunctions in feeding behavior, increasing vulnerability to palatable food consumption. OO intake during pregnancy and lactation counteracted some stress-induced effects, suggesting its potential to modulate and sometimes attenuate the adverse outcomes of early-life stress.

Funding:
National Council for Scientific and Technological Development (CNPq - Brasil)

Key-words: (up to 5):
feeding behavior; maternal separation; olive oil; male and female rats.

Resumen #00004960 en

Impact of breastfeeding on liver metabolic dysfunction in offspring born from hyperglycaemic dams in a rodent model.

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Paul Bobin (1), Blandine Castellano (1), David-Sochard Agnès (1), Croyal Mikaël (1), Raux Axel (2), Darmaun Dominique (1), Le Dréan Gwénola (1), Alexandre-Gouabau Marie Cécile F. (1)
(1) INRAE, (2) ONIRIS

Background/aims:
Gestational Diabetes Mellitus (GDM) induces lasting metabolic programming in offspring, increasing their risk for insulin resistance and metabolic dysfunction-associated steatotic liver disease (MASLD). MASLD-rising incidence in youth suggests early-life origins, potentially shaped by maternal metabolic status during gestation and lactation, and also breastfeeding and sex-specific factors. This study investigates how GDM affects maternal transmission of MASLD-risk, focusing on breast milk contribution.

Methods:
A rodent GDM-model was developed using a high-fat high-sucrose (HFHS) diet to induce impaired glucose tolerance (IGT) limited to gestation (4HFHS) or maintained throughout gestation-lactation (7HFHS), compared to a control-fed euglycemic group (CTL). Cross-fostering at birth allowed to assess the independent impact of gestation versus lactation. Offspring underwent body composition analysis using dual-energy X-ray absorptiometry at postnatal day (PND) 200. Insulin-sensitivity was evaluated at PND 220, through oral glucose tolerance test and euglycemic-hyperinsulinemic clamp following a Western-Diet (WD) challenge (100d). Metabolome (LC-MS) and transcriptome (qRT-PCR) were analyzed in offspring blood and liver.

Results:
Male GDM-offspring nursed by 7HFHS-dams and WD-fed at adulthood exhibited the highest fat mass and liver weight, compared to other WD-groups or their chow-fed counterparts. This phenotype was associated with disrupted lipid metabolism including incomplete fatty acid oxidation (FAO), increased cholesterol synthesis, reduced polyunsaturated fatty acid synthesis and incorporation in triglycerides or phosphatidylcholines. GDM-offspring nursed by CTL-dams and WD-fed displayed IGT (male) and lower insulin-sensitivity (female), lower FAO, combined with higher hepatic expression of glucose and lipid transporters, and FETUA, an insulin-resistance biomarker. In contrast, GDM-offspring reared by 4HFHS-dams showed improved FAO, reduced gluconeogenesis and lipogenesis (essentially in females), but better insulin receptor and lower FETUA expression.

Conclusions:
GDM and lactational exposure significantly influence liver metabolic programming in offspring in a sex-specific manner. GDM-related milk components may act as early modulators of MASLD-risk, highlighting breastfeeding as a critical window for potential postnatal intervention.

Funding:
ANR-22-CE17-0039-GDM-MILK ; INRAE AlimH ; Région Pays de la Loire ; Société Française de Néonatologie Ethical considerations:

The authors certify that the conditions for submission have been satisfied and that all animal welfare and ethical considerations have been met.

The experimental protocol was carried out in accordance with current institutional guidelines on animal experimentation in the EU (directive 2010/63/EU) and in France (French Veterinary Department—A44276) and the 3Rs (Replacement, Reduction, Refinement) principle. All animal procedures were approved by the Animal Ethics Committee of Pays de La Loire and the approval from the French Ministry of Superior Education and Research (APAFIS #35043-202201131758975 9v6)"

Key-words: (up to 5):
Gestational Diabetes Mellitus, Lactation, Metabolomics, MASLD

Resumen #00004616 en

The genetic aetiology of high and low birthweight and its relationship with cardiometabolic disease

Mechanisms Determining Transgenerational Effects of Health and Disease

Evans David (1), Hwang Liang-Dar (1), Brito Nunes Caroline (1), Warrington Nicole (1), Moen Gunn-Helen (1) (1) University of Queensland

Background/aims:
Recent genome-wide association studies(GWAS) have suggested that the inverse correlation between birthweight and cardiometabolic disease is driven by genetic and not environmental factors. However, previous GWAS have focused on individuals within the “normal range” of birthweight. Our aim was to investigate if the genetic factors operating at the extremes of birthweight were different to those explaining variation within the normal range, to explore the genetic correlation between extremes of birthweight and cardiometabolic disease, and to investigate whether analyzing extreme birthweights improved ability to detect genetic loci.

Methods:
We performed GWAS analysis of low(<2.5kg) and high(>4.5kg) birthweight in the UK Biobank(Nlow=20,947; Nhigh=12,715; Ncontrols=207,506) and conducted three continuous GWAS of birthweight, one including the full range of birthweights, one involving a truncated GWAS including only individuals with birthweights between 2.5 and 4.5kg, and a third that winsorized extreme values. All conditions for abstract submission were satisfied and ethical approval for the study.

Results:
High birthweight had a similar genetic aetiology to birthweight within the normal range(rG=0.91, SE=0.04), whereas there was evidence for a separate set of genes underlying low birthweight(rG=-0.74, SE=0.04). Low birthweight was positively genetically correlated with most cardiometabolic traits and diseases, whereas high birthweight was mostly positively genetically correlated with adiposity and anthropometric related traits. The winsorization strategy performed best in terms of locus detection doubling the number of significant associations including 25 novel loci. This included a low frequency missense variant in ABCC8, a gene involved in congenital hyperinsulinism, neonatal diabetes mellitus and mature onset diabetes of the young that was estimated to be responsible for a 170 gram increase in birthweight amongst carriers.

Conclusions:
Genetic factors are responsible for much of the inverse phenotypic correlation between birthweight and many cardiometabolic traits and diseases.

Funding:
D.E. and this work are funded by an Australian National Health and Medical Research Council Investigator grant (APP2017942) and Ideas grant (GNT1183074). G.M. is the recipient of an Australian Research Council Discovery Early

Career Award (Project number: DE220101226) funded by the Australian Government and supported by the Research Council of Norway (Project grant: 325640). L.H. is funded by an Australian Research Council Discovery Early Career Researcher Award (DE240100014). N.W is funded by an Australian National Health and Medical Research Council Investigator Grant (APP2008723).

Key-words: (up to 5):
Birthweight, Cardiometabolic disease, GWAS, DOHaD, Genetics

Resumen #00005046 en

Associations of Cord Blood Insulin-Like Growth Factors (IGF), IGF-Binding Proteins, Leptin, and Adiponectin Levels with Childhood Overweight/Obesity and Adiposity

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

CHEN ZILIN (1), Luo Zhong-cheng (2)
(1) Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, (2) Department of Obstetrics and Gynecology, Mount Sinai Hospital

Background/aims:
Early-life environment may “program” early childhood obesity, yet the early-life prognostic biomarkers remain unclear. The aim of this study was to evaluate whether cord blood leptin, adiponectin and fetal growth factors are related to obesity/adiposity in early childhood.

Methods:
In a nested case–control study of 120 pairs of overweight/obesity and optimal-weight children in the Shanghai Birth Cohort, we accessed cord plasma concentrations of IGF-1, IGF-2, IGFBP-1, IGFBP-2, IGFBP-3 leptin, total adiponectin, and high-molecular-weight (HMW) adiponectin in relation to obesity/overweight and adiposity indicators [body mass index (BMI z score), body fat mass (BFM), and percent body fat (PBF)] in early childhood at age 4 years.

Results:
Comparing overweight/obese vs. optimal weight children, cord blood concentrations of IGF-1 (85.59±44.57 vs. 64.37±31.04 ng/ml, P < 0.001) were higher, but IGFBP-1 (59.27±110.69 vs. 76.14±124.15 ng/ml, P = 0.03) , total adiponectin (33.36±15.37 vs. 37.50±16.09 μg/mL, P = 0.04) and HMW adipokines
(16.81±9.84 vs. 19.82±12.19 μg/mL, P = 0.05) were lower. Cord blood IGF-1 was positively, while IGFBP-1, IGFBP-2, and high-molecular-weight adiponectin were negatively correlated with BMI z score in children at age 4 years. Higher cord blood IGF-1 was associated with an increased risk of childhood overweight/obesity at age 4 years (adjusted OR 2.06, 95% CI: 1.16-3.65 per log unit increase). Higher cord blood total adiponectin was associated with a reduced risk of childhood overweight/obesity (adjusted OR
0.48, 95% CI: 0.25-0.93).

Conclusions:

Our research was the first to reveal the associations between cord blood fetal growth-related molecules and obesity/adiposity in early childhood. High IGF-1 and low adiponectin in cord blood may serve as potential early life prognostic biomarkers of childhood overweight/obesity.

Funding:
the Ministry of Science and Technology of China (2019YFA0802501), the National Natural Science Foundation of China (82430104, 82125032 and 81930095)

Key-words: (up to 5):
Obesity, early childhood, cord blood, Adiponectin, IGF-1

Resumen #00005276 en

Human milk oligosaccharides (HMOs) clusters within 3 months postpartum associate with neurobehaviour in early childhood in the Asian GUSTO cohort

Role of Infant and Young Child Feeding Practices on Long-Term Health

Zhang Han (1), Lim Yu Xian (1), Spann Kennedy (2), Wee Charlene (1), Ang Li Ting (1), Pang Wei Wei (3), Wong Chun Hong (1), Chua Mei Chien (4), Cai Shirong (1), Shek Lynette P. (3), Chong Yap Seng (3), Yap Fabian (4), Tan Kok Hian (4), Lee Yung Seng (3), Broekman Birit F. P. (5), Geddes Donna (6), Wlodek Mary E (7), Bode Lars (2), Chan Shiao-Yng (3)

(1) Institute for Human Development and Potential (IHDP), A*STAR, Singapore, (2) Department of Pediatrics and the Human Milk Institute (HMI), University of California San Diego, USA, (3) Yong Loo Lin School of Medicine, National University of Singapore, Singapore, (4) Duke-NUS Medical School and KK Women's and Children's Hospital, Singapore, (5) Department of Psychiatry, Amsterdam UMC, Vrije Universiteit Amsterdam, The Netherlands, (6) School of Molecular Sciences, The University of Western Australia, Australia, (7) Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Australia

Background/aims:

Studies on HMOs (bioactive human milk carbohydrates) and neurodevelopment have shown inconsistency, possibly due to population differences in HMO profiles, metabolism, and offspring responses. Most research employed non-Asian populations and rarely considered secretor status. Hypothesizing that HMOs collectively influence child neurobehaviour, we aimed to associate naturally-occurring HMO clusters with early childhood cognition and behaviour in a Singapore Asian cohort comprising Chinese, Malay and Indian participants.

Methods:

Nineteen HMOs were quantified in samples collected at 3-weeks and 3-months postpartum from 248 mothers in the GUSTO mother-offspring cohort. Latent profile analysis of HMO data determined maternal groupings accorded with secretor (Se) and lewis (Le) status. With the largest group, Se+/Le+ (n=160), exploratory factor analysis (EFA) identified naturally-occurring HMO clusters. Cognition (Bayley-III, CANTAB-Spatial-Working-Memory) and behaviour (CBCL/1.5-5) were assessed at 2 and 4 years (y), with scores pre-adjusted for maternal education, parity, antenatal maternal mood, and gestational tobacco-exposure. Associations between HMO clusters and neurobehaviour were examined by regression, adjusting for ethnicity, sex, gestational age at delivery, birthweight, and breastfeeding duration >1-month.

Results:

Among Se+/Le+ mothers, EFA identified 4 mutually-exclusive HMO clusters (total 62.9% variance explained). Increasing concentrations of the HMO cluster (FDSLNH, LNFP-II, LNH, and 3FL; 15.8% variance explained) were associated with better language (0.26SD [0.03,0.48]; p=0.03) and motor skills (0.26SD [0.03,0.48]; p=0.03) at 2y. Another HMO cluster (LSTb, DSLNT, and DFLNT; 11.9% variance explained) was associated with less total behavioural problems (0.30SD [0.02,0.58]; p=0.03) at 2y and better working memory (0.33SD [0.13,0.54]; p=0.002) at 4y. However, a separate HMO cluster (DSLNH, LSTc, and 6'SL;

14.8% variance explained) was associated with poorer language skills at 2y.

Conclusions:

This study suggests that HMOs consumed in early infancy may collectively influence neurodevelopment. Our findings present patterns opposite to those reported in other cohorts, cautioning against extrapolating HMO understanding across ethnically and geographically diverse populations.

Funding:
Singapore National Research Foundation under its Human Potential Program (H23P1M0004)

Key-words: (up to 5):
human milk oligosaccharides, secretor status, cognition, behavioural problems, early childhood

Resumen #00005409 en

Fetal origins of persistent vascular sympathetic hyper-reactivity in offspring of obese pregnancy

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Cochrane Anna (1), Davison Skaai (1), Crew Rachael (1), Niu Youguo (1), Ford Sage (1), Cahen Clement (1), Murphy Michael (1), Ozanne Susan (1), Giussani Dino (1)
(1) University of Cambridge

Background/aims:
Obesity during pregnancy increases the cardiovascular risk in adult offspring. However, whether this originates in fetal life, and underlying mechanisms, remains under-investigated. We tested the hypothesis that maternal obesity in pregnancy induces fetal cardiovascular dysfunction, which persists into adulthood.

Methods:
Procedures were performed under ASPA 1986 Amendment Regulations 2012. Ewes were fed 60 days pre-conception and throughout gestation a control diet (C, 200 g/day concentrates and ad libitum hay, n≥6) or obesogenic diet (OB, ad libitum concentrates and hay, n≥10). At 117±2 days gestational age (dGA; term ~145 days), under general anaesthesia, catheters and Transonic flow-probes were placed in fetal carotid and femoral arteries. At 122±3 dGA, hypoxia was induced for 30 min (maternal FiO2 7.5%). At 130±2 dGA, fetal femoral resistance arteries were isolated for wire myography. A second un-instrumented cohort delivered spontaneously at term, offspring weaned at 3 months and fed a control diet thereafter. At 9 months, pressor responses to phenylephrine (i.a.) were determined via a femoral catheter implanted a week earlier under general anaesthesia. Data (mean±SEM) were analysed with the Student's t-test or 2-way ANOVA.

Results:
OB fetuses showed enhanced increases in blood pressure and femoral vascular resistance during hypoxia (both Pdiet<0.0001). Greater increments in fetal plasma cortisol during hypoxia (C vs. OB, +3.26±2.02 vs. +12.01±2.50 ng.mL-1) and femoral vasoconstriction to phenylephrine ex vivo (41.4±8.7 vs. 74.4±11.6 %Kmax) contributed to mechanisms (all P<0.05). OB adult offspring were hypertensive (85.6±2.0 vs. 95.7±2.47 mmHg) and showed greater blood pressure increments to phenylephrine doses in vivo
(+9.8±3.0 vs. +16.7±2.7 mmHg; both P<0.01), an effect driven by males (+190%) more than females (+36%).

Conclusions:
Maternal obesity in pregnancy promotes vascular sympathetic hyper-reactivity in offspring. The phenotype originates in fetal life and promotes hypertension in adulthood, supporting a prenatal origin in the cardiovascular risk in offspring of obese pregnancy.

Funding:
MRC and BHF

Key-words: (up to 5):
Maternal obesity, cardiovascular

Resumen #00003845 en

Perineuronal nets and oligodendrocyte maturation as mediators of hypothalamic development

Role of Infant and Young Child Feeding Practices on Long-Term Health

Lomniczi Alejandro (1), Bitar Joelle (1), Watson Katherine (1), MacKinnon Riley (1) (1) Dalhousie University

Background/aims:
In atricial animals like rats and mice, there is a critical perinatal period during which metabolic alterations can affect the development of hypothalamic kisspeptin neurons resulting in variations of the timing of puberty. Here we aim at identifying the molecular signatures of metabolically induced changes in hypothalamic developmental trajectories.

Methods:
We used a model of undernutrition by raising female Wistar rats in large litters (LL:18 pups/dam) starting at postnatal day 0 (P0), overnutrition was achieved by raising rats in small litters (SL: 3 pups/dam), while control animals were raised in normal litters (NL: 12 pups/dam). Pubertal timing was determined as the day of first estrus. Gene expression was obtained RNA sequencing of the arcuate nucleus-median eminence (ARC-ME) at P14 followed by a battery of systems biology approaches. Gene expression data at P14-28 were validated by qPCR. Immunofluorescence of perineuronal nets (PNNs) was performed using biotinylated Wisteria Floribunda lectin. Mature oligodendrocytes (OL) were detected with Myelin Basic Protein (MBP) staining, in colocalization with Kisspeptin and GnRH neurons.

Results:
Overnourished (SL) rats showed advanced puberty, increased Kiss1 expression and Kiss1 neuron arborization. Undernourished (LL) rats showed delayed puberty, reduced Kiss1 expression and Kiss1 neuron arborization. RNAseq analysis of the ARC-ME showed altered Gene Ontology Pathways including Extracellular matrix formation, Cell proliferation and Differentiation of OLs. Single cell transcriptome indicated an enrichment of genes involved in OL development and maturation as well as cells implicated in assembly of PNNs. Staining of PNNs showed a marked increase in ARC-ME density in SL and a reduction in LL animals. Moreover, MBP staining showed enhanced OL maturation in SL and diminished in LL animals.

Conclusions:
Early-life nutritional alterations disturb hypothalamic OL and PNN developmental trajectories impacting Kisspeptin neuron connectivity and pubertal maturation.

Funding:
NIH HD084542, NIH AG061141 and Startup funds from Dalhousie University.

Key-words: (up to 5):
Perineuronal nets, kisspeptins, puberty, oligodendrocytes

Resumen #00003527 en

Impact of Mid-Gestation Maternal Supplementation on Testicular Maturation and Sperm Quality in Lambs at 140 Days

Plant and Animal Health and Its Impact on Reproductive Age Individuals and Their Offspring

Pedrana Graciela (1), Viotti Helen (1), Mernies Beatriz (1), Folgar Lilena (1), Cambruzzi Javier (1), Balemián Nariné (1), Delmiro William (1), Lombide Paula (1), Rodriguez Osorio Nélida (2), Martin Graeme (3)
(1) Facultad de Veterinaria, Universidad de la República, (2) Centro Regional litoral noroeste, Universidad de la República, (3) University of Western Australia

Background/aims:
In pregnant female sheep, high levels of nutrition during gestation and lactation will increase the number of Sertoli cells and the diameter of sexual cords/seminiferous tubules in lambs. We tested whether that enhanced maternal nutrition during mid gestation only will also improve the initiation and progression of spermatogenesis.

Methods:
The experiment was approved by the Animal Ethics Committee of the Veterinary Faculty, University of the Republic (CEUA FVET-1737-111900-000043-23). Pregnant ewes were randomly assigned to either a control group (natural pasture only, n = 20) or a group fed natural pasture plus a supplement from day 70 of gestation until birth (n = 20). After birth, male lambs (n = 12 per group) remained with their mothers on natural pasture until age 140 days when testicular tissue was collected for histological assessment of Stage VI of the spermatogenic cycle (before spermiation). Semen was also collected from a cauda epididymis and subjected to the Hypo-Osmotic Swelling Test (HOST) and Eosin-Nigrosin staining. Chi-squared analysis was used to assess differences between the groups.

Results:
Compared to the control group, the supplemented group had a greater percentage at Stage VI of the spermatogenic cycle (27% versus 17%; P = 0.05). Conversely, the supplemented group had fewer eosin-nigrosin-positive sperm (27% versus 40%; P = 0.001) and more HOST-positive sperm (30% versus 17%; P = 0.001), relative to the control group.

Conclusions:
Mothers that were supplemented during gestation produced male lambs with enhanced post-meiotic spermatogenesis, and fewer epididymal spermatozoa displaying plasma membrane abnormalities. Maternal nutritional supplementation from mid-gestation therefore enhances the postnatal testicular development of male offspring, promotes the progression of spermatogenesis, and improves epididymal sperm membrane quality. Clearly, targeted maternal nutrition is needed to optimize reproductive performance in livestock production systems.

Funding:
Full-Time, Dra. Graciela Pedrana Régimen de Dedicación Total, Universidad de la República.

Key-words: (up to 5):
nutritional, fetal-programming, reproduction, spermatogenic-cycle

Resumen #00005060 en

Prenatal depressive symptoms influence offspring neurodevelopment through maternal gut microbiota during pregnancy

Mechanisms Determining Transgenerational Effects of Health and Disease

Zhou Fangyue (1)
(1) Obstetrics and Gynecology Hospital of Fudan University, Shanghai, China

Background/aims:
Few human studies have investigated the impact of prenatal depression (PND) on maternal gut microbiota during pregnancy. Furthermore, the underlying mechanisms by which PND symptoms may influence offspring neurodevelopment via the gut microbiota await further exploration.

Methods:
Based on the multicenter prospective cohort study “Sino-Canadian Healthy Life Trajectories Initiative”, fecal samples were collected from pregnant women with PND symptoms (EPDS ≥10) and control group (with EPDS <10) across different trimesters for 16S rRNA sequencing analysis. Offspring neurodevelopment were longitudinally assessed by ASQ-3 at multiple timepoints within the first year of life, and the correlation between PND-associated maternal gut microbiota and offspring neurodevelopmental outcomes was analyzed. Additionally, a germ-free dam human fecal microbiota transplantation model was established to investigate the impacts of PND-associated microbiota transplantation on cognitive function in offspring mice.

Results:
A total of 135 participants were included in each of the PND and the control group. Offspring in the PND group exhibited significantly lower problem-solving ability (P = 0.020). PND symptoms exerted a significant impact on the composition of maternal gut microbiota throughout pregnancy. The abundance of SCFAs-producing bacteria, such as Eubacterium was markedly reduced. Additionally, PND symptoms were associated with dysregulated amino acid metabolism in maternal gut microbiota. Furthermore, PND-associated maternal gut microbiota dysbiosis showed significant correlations with poorer offspring neurodevelopment. Morris water maze tests revealed that offspring of germ-free dams transplanted with PND-associated microbiota displayed significant cognitive impairment, accompanied by disrupted metabolism of polyunsaturated fatty acids and amino acids in fetal brains.

Conclusions:
PND symptoms may disrupt offspring neurodevelopment by altering the composition and functionality of maternal gut microbiota, leading to dysregulated metabolism of polyunsaturated fatty acids and amino acids in the fetal brain, which subsequently impairs postnatal cognitive function.

Funding:
National Natural Science Foundation of China 82261128001

Key-words: (up to 5):
Prenatal depression, Gut microbiota, Neurodevelopment

Resumen #00005826 en

The Flourishing in Fatherhood Project: psychosocial and physiological health of Australian fathers

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Gibson Lisa Yvonne (1), Silva Desiree (1), Segers Emily (1), Davis Jackie (1), Whalan Sarah (1), Yeap Bu (2) (1) The Kids Research Institute Australia, (2) The University of Western Australian

Background/aims:
The physical and psychological health of expectant and new fathers is poorly understood. Previous research shows that fathers have an increased risk of cardiometabolic disease and poorer mental health comparative to childless counterparts. The Flourishing in Fatherhood Project aims to deepen our understanding of father's physical and psychosocial health and also gain an understanding of father's experiences of the transition to fatherhood and what supports they need during this time.

Methods:
Fathers participating in ORIGINS, a longitudinal birth cohort in Perth, Western Australia, were invited to participate. Fathers attended a face-to-face appointment to assess their cardiovascular and metabolic health (cholesterol, blood pressure, blood sugar, smoking, exercise). Participants also completed online questionnaires assessing their psychosocial wellbeing (mental health, family and marital functioning, parenting styles and work/family balance). A sub-set of fathers (N= 12) participated in focus groups to understand their experience of antenatal care and the transition to fatherhood.

Results:
Between July 2023 and April 2025 303 fathers attended the appointments and completed the questionnaire. 77% (235/303) of participants had a BMI >24.9 classifying them as overweight and obese. 61% (186/303) of participants had a waist girth ≥ 94cm (61%). While over half of the fathers didn't meet recommended weekly physical activity recommendations. The focus groups highlighted that many of the fathers felt excluded from antenatal appointments and felt this was a barrier to equitable participation in parenting and decision-making, specifically during pregnancy and the birth.

Conclusions:
The findings from the Flourishing in Fatherhood Project are intended to promote greater inclusion of fathers into antenatal care schedules, while gaining an understanding on how best to improve the health of fathers over the long term through healthy lifestyle interventions.

Funding:
This project is funded by a HBF Health Fund Community partnership grant.

Key-words: (up to 5):
psychosocial health, fatherhood, cardiovascular health, healthy lifestyles

Resumen #00006048 en

Time-Course Analysis of Early High-Sucrose Diet Exposure on Cognitive Performance in Weaned Rats.

Role of Infant and Young Child Feeding Practices on Long-Term Health

MELO THAMYS MARINHO (1), OLIVEIRA LÚCIA CASTRO SANTOS DE (1), RODRIGUES NATHALIA KESSIA CORRÊA (1), ALENCAR MAYSA SOUZA DE (1), RIBEIRO RAFAEL DO CARMO SILVA (1), MACEDO BRUNO EDUARDO LOPES DE (1),
FRANÇA LUCAS MARTINS (1), PAES ANTONIO MARCUS DE ANDRADE (1), PINTO BRUNO ARAÚJO SERRA (1) (1) UFMA

Background/aims:
The DOHaD hypothesis emphasizes the importance of early-life nutrition for long-term health outcomes. In Latin America, excessive sugar intake during infancy and childhood is a current concern, which may affect hippocampal circuits leading to cognitive deficits. Thus, this study aimed to investigate the time-course of excessive sucrose consumption on cognitive performance in weaned rats.

Methods:
Weaned Wistar rats (55.98 ± 0.94 g) were assigned to either control (CTR, n=15) or high-sucrose diet (HSD, n=15) groups, receiving standard chow (10% sucrose) or HSD (25% sucrose) for 30, 60, or 90 days (n=5/group/time). Spatial memory was assessed during the last week of each period using the Morris water maze. Behavioral data were analyzed with ToxTrac and GraphPad Prism 8.0 (CEUA UFMA nº 23115.016728/2024-47).

Results:
After 30 days, the DRS group showed learning impairments, evidenced by a higher area under the curve during the training phase (63.07 ± 7.658 vs. 41.53 ± 7.658; p = 0.0102) and reduced spatial memory in the probe trial (44.67 ± 4.513 vs. 54.63 ± 4.513 s; p = 0.0315). At 60 days, learning deficits persisted, accompanied by a significant reduction in average swimming speed (87.59 ± 3.272 vs. 100.1 ± 3.272 mm/s; p = 0.0025), suggesting early motor impairment, while memory impairments became more pronounced. After 90 days, cognitive deficits worsened for both learning (AUC: 58.42 ± 4.236 vs. 44.09 ± 4.236; p = 0.0035) and memory (35.02 ± 5.162 vs. 45.70 ± 5.162 seconds; p = 0.0361), although no significant changes in locomotor performance were observed.

Conclusions:
Excessive sucrose intake during early life led to sustained impairments in spatial learning and progressively worsening memory deficits up to 90 days. These findings support the DOHaD hypothesis and underscore the lasting impact of early unhealthy nutritional exposures on long-term cognitive health.

Funding:
CAPES, CNPq, and FAPEMA.

Key-words: (up to 5):
Sucrose; Cognitive impairment; Early-life nutrition; Spatial memory; Neurodevelopment.

Resumen #00005710 en

Maternal High-Fat and High-Sucrose Diets Differentially alter Mammary Gland Adiposity, Milk Lipid Composition and Offspring Adiposity

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Baqueiro Mayara (1), Nascimento Luciana (2), Silva Maiara (2), Alves Lavinia (2), Torsoni Marcio (2), Ross Michael (3), Desai Mina (3), Torsoni Adriana (2)
(1) UNICAMP/UCLA, (2) University of Campinas (UNICAMP) , (3) The Lundquist Institute at Harbor-UCLA Medical Center

Background/aims:
Both developmental and lactational programming influence offspring adiposity. Breast milk composition is impacted by maternal obesity and diet. As Western diet includes high levels of fat and sucrose, we investigated their effects on mammary tissue adiposity and lipid metabolism, milk lipid composition and offspring adiposity.

Methods:
Female mice were fed either a control (CT, n=14; 10%fat, 7%sucrose), high-sucrose (HS, n=27; 10%fat, 35%sucrose) or high-fat diet (HF, n=22; 45%fat, 17%sucrose) before and during pregnancy and lactation. Mammary tissue was collected at gestation age e19 and at end of lactation day p21 for adipocyte area (H&E staining) and mRNA expression (RT-qPCR) of genes associated with lipid metabolism and inflammation. Milk was collected on day p12 of lactation and lipid profile undertaken (MRM mass spectrometry). ANOVA with Bonferroni-test was used.

Results:
At e19, HF dams had higher mammary adipocytes area than HS and CT, while at p21, HS had greater mammary adipocytes area than CT. Adipocyte area in mammary tissue decreased more in HF (18.6%) and CT (23.7%) than HS (2.5%). At p21, long-chain acyl-CoA dehydrogenases (Acadvl, essential for fatty-acid oxidation) and pro-inflammatory cytokine (Il1b) expression was higher in HF compared to HS and CT. HF dams milk showed an increased proportion of polyunsaturated and lower monounsaturated triglycerides than HS and CT. In contrast, milk from HS dams had higher proportion of saturated triglycerides than HF. At p21, HF and HS female and HF male offspring showed increased body weight and fat mass compared to their respective CT. Maternal body weight and offspring weight gain were positively correlated with mammary adipocyte area.

Conclusions:
The findings suggest that maternal HF and HS diets differently affect adiposity and mammary lipid metabolism, leading specific changes in milk composition. Improving maternal diet during critical developmental periods may help prevent future metabolic dysfunction in future generations.

Funding:
NIH grant #R01HD099813 **Key-words: (up to**

5):

High-Fat-Diet,High-Sucrose-Diet,Metabolic-Programming,Milk, Offspring

Resumen #00004979 en

Neonatal hyperoxia disrupts left ventricular vascular development and promotes maladaptive remodeling linked to adult cardiovascular dysfunction.

Impact of Early Life Exposures and Environmental Pollutants

Girault-Sotias Pierre-Emmanuel (1), Ravizzoni Dartora Daniela (1), Pedro Henrique Mayrink (1), De Sousa Do Outeiro Coraline (1), Irgolitsch Frans (2), Brun Oliver (2), Deprez Alyson (1), Poletto Bonetto Jéssica Hellen (1), Cloutier Anik (1), Lesage Frédéric (2), Jankov Robert Peter (3), Luu Thuy Mai (1), Nuyt Anne Monique (1)
(1) CHU Sainte-Justine Azrieli Research Center , (2) Polytechnique Montréal, (3) CHEO Research Institute

Background/aims:
Prematurity (PT) is associated with increased cardiovascular disease risk in adulthood. We previously demonstrated that neonatal hyperoxia induces long-term cardiac dysfunction in rats (Oxygen-Induced Cardiomyopathy, OIC). While premature birth has been linked to systemic vascular alterations, its impact on left ventricular (LV) vascularization remains unclear. This study aimed to characterize coronary and capillary morphology and associated molecular programs, in the OIC model.

Methods:
Sprague Dawley pups were exposed to 80% O_2 (OIC) or room air (CTRL) from postnatal day 3 (P3) to P10. Hearts were collected at P10, 4 weeks, and 16 weeks. All experiments were approved by the ethics committee (#2023-5111). Capillary density, and 3D vascular architecture were quantified. Expression of pro-angiogenic factors was assessed by RT-qPCR and Western blot. Results (mean±SEM; Ctrl vs OIC) are compared using t test (N = 6/group).

Results:
P10 males, OIC rats showed decreased capillary density (0.63±0.05vs.0.71±0.02mm²), shorter coronary segments (77.9±0.12vs.83.3±0.08µm), and reduced diameter (45.4±0.04vs.49.2±0.03µm), despite increased VEGFA (76%) and NRP1 (38%). At 4 weeks, OIC group showed increased arteriolar length (101.2±0.18vs.95.5±0.20 µm) and diameter (49.7±0.07vs.51.2±0.11 µm), while decreased VEGFA (14%) with unchanged capillary density. At 16 weeks, cardiomyocyte hypertrophy was observed, with increased capillary density (1.37±0.03vs.0.98±0.07 mm²) and downregulation of VEGFA (23%), VEGFR1 (27%), VEGFR2 (20%), and NRP1 (17%).

Conclusions:
Neonatal hyperoxia disrupts early coronary vascular development and induces long-term maladaptive remodeling. Initial capillary rarefaction, despite elevated VEGFA, suggests failed angiogenesis. Later remodeling, including hypertrophy and receptor downregulation, may underlie increased cardiovascular risk after prematurity.

Funding:
Fondation CHU Sainte-Justine, Société québécoise d'hypertension artérielle, Fonds de Recherche du Québec - Santé (#343017), Molly Towell Perinatal Research Foundation

Key-words: (up to 5):
Prematurity, Neonatal hyperoxia, Coronary vasculature, Cardiac remodeling, Angiogenic signaling

Resumen #00005932 en

Fetal Cardiac Remodeling and Functional Alterations in the Offspring of Women with Pregestational Obesity

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Araujo Kenny (1), Carrasco-Nogue Karina (2), Moya Jackeline (2), Carvajal Jorge (2), Crispi Fátima (3), Casanello Paola (4)

(1) Pontificia Universidad Católica de Chile, (2) Departamento de Obstetricia, Facultad de Medicina, Pontificia Universidad Cato´lica de Chile, (3) BCNatal (Hospital Clínic and Hospital Sant Joan de Deu), IDIBAPS, Universidad de Barcelona, (4) Pontificia Universidad Cato´lica de Chile

Background/aims:
Maternal obesity is a recognized risk factor for the developmental origin of cardiovascular disease in the offspring. However, its effects on fetal cardiac structure and function remain insufficiently explored. We aimed to assess the impact of maternal obesity on fetal cardiac development.

Methods:
This analysis was conducted within the OMEGA-STEM trial (FONDECYT #1221812), including pregnant women with normal weight (NW, BMI 18.5–24.9 kg/m²) and pregestational obesity (PO, BMI ≥30 kg/m²). At 32–36 weeks of gestation, participants underwent fetal biometry, fetoplacental Doppler, and comprehensive 2D, M-mode, and Doppler echocardiographic assessments to evaluate cardiac structure, morphometry, and function. Cardiovascular parameters included cardiac dimensions, systolic and diastolic function, aortic intima-media thickness, and epicardial fat. All participants provided written informed consent (Institutional Ethics Committee #230515004).

Results:
A total of 78 fetal echocardiograms were performed (54 NW and 24 PO). Prepregnancy BMI (33.76 ± 3.12 vs 22.66 ± 1.7 kg/m², p<0.05) was higher in PO, and gestational age at assessment (33.97 ± 1.54 vs 33.79 ± 1.4 weeks) was similar between groups. Fetuses of pregnant women with PO exhibited greater interventricular septal thickness (3.59 ± 0.46 vs 3.20 ± 0.45 mm, p=0.01), larger right atrial area (2.61 ± 0.52 vs 2.19 ± 0.39 cm², p=0.004), and increased right ventricular basal and longitudinal diameters. The aortic intima-media thickness was significantly higher in fetuses of PO women compared to NW (0.04±0.01 vs 0.05±0.01, p=0.006).
Ductus venosus pulsatility index was higher in fetuses of PO women compared to NW (0.55 ± 0.16 vs 0.45 ± 0.16, p=0.04). Right and left ventricular fractional area change tended to be lower in fetuses of mothers with obesity.

Conclusions:

Maternal obesity is associated with fetal cardiac remodeling and early signs of altered cardiac function. Further longitudinal studies are needed to determine whether these changes persist postnatally and their long-term clinical significance.

Funding:
FONDECYT #1221812, ANID BECAS/DOCTORADO NACIONAL 21221138

Key-words: (up to 5):
Fetal heart, cardiovascular programming, Cardiac remodeling

Resumen #00004491 en

Children of UPBEAT: Child heart structure and function 10-years after the UPBEAT lifestyle intervention in obese pregnancy

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Burden Samuel (1), Kaur Simrat (1), Alshehri Rahaf (2), Vasa Ernestene (2), Gill Carolyn (1), Villar Leyre (3), Nelson Scott (4), Sattar Naveed (5), Anderson Mark (6), Perchard Reena (7), Fiori Federico (8), Santosh Paramala (8), Sinha Manish (9), Gu Haotian (2), Poston Lucilla (1), Taylor Paul (1), on behalf of the UPBEAT consortium . (10)
(1) Department of Women and Children's Health, King's College London, (2) Cardiovascular Medicine and Science Research, King's College London, (3) University Hospital Carl Gustav Carus, Dresden, (4) School of Medicine, Dentistry and Nursing, Reproductive and Maternal Medicine, University of Glasgow, (5) School of Cardiovascular and Metabolic Health, University of Glasgow, (6) Department of Paediatric Medicine, The Newcastle upon Tyne Hospitals NHS Foundation Trust, (7) Division of Developmental Biology and Medicine, University of Manchester, (8) Institute of Psychiatry, Psychology and Neuroscience, King's College London, (9) Department of Paediatric Nephrology, Evelina London Children's Hospital, (10) King's College London

Background/aims:
Children exposed to maternal obesity in pregnancy are more likely to develop adult cardiovascular disease. There is evidence that diet and lifestyle interventions during obese pregnancy can limit the degree of changes in heart structure and function, but existing studies are limited to small cohorts of younger children. Here, we present an interim analysis from a 10-year cardiovascular follow-up of children from the UK Pregnancies Better Eating and Activity Trial (UPBEAT).

Methods:
A cross-sectional, longitudinal follow-up study of 9–14-year-old children from UPBEAT was conducted in four centres across the UK (London, Glasgow, Manchester, Newcastle; Ethics Committee #23/LO/0410). Children had cardiac structure and function assessed by echocardiography, vascular stiffness by B-mode ultrasound and applanation tonometry, and blood pressure and heart rate variability by 36-hour ambulatory wearable devices.

Results:
An interim analysis of n=100 children found that the UPBEAT intervention reduced interventricular septal wall thickness (IVS: -0.06cm, p=0.002), IVS z-score (-0.39, p=0.003), relative wall thickness (-0.02, p=0.054), and increased peak septal wall early diastolic myocardial velocity (e': +0.8cm/s, p=0.023). There were differences in asleep ambulatory HRV (low frequency power, p=0.049; high frequency power, p=0.029; LF/HF ratio [indicative of reduced sympathovagal balance], p=0.038). There were no apparent differences in ambulatory blood pressure, or other echocardiography, vascular stiffness, or HRV measures between the UPBEAT intervention and standard care arms. As of 18th April 2025, n=160 participant visits have been completed. At the DOHaD 13th World Congress, we will present updated results from n>200 children.

Conclusions:
Preliminary findings indicate that the UPBEAT lifestyle intervention in obese pregnancy reduces the degree of cardiovascular remodelling and autonomic dysfunction in 9–14-year-old children, which if sustained until adulthood, could provide primordial prevention against adult cardiovascular disease.

Funding:

British Heart Foundation (SP/F/21/150013).

Key-words: (up to 5):
obesity

Resumen #00005758 en

Insulin-induced High Fat Breast Milk is Normalized by Metformin: Use of 3-dimensional Mammary Epithelial Cell Culture

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Desai Mina (1), Han Guang (1), Rao Krishna (2), Ross Michael (1)
(1) The Lundquist Institute at Harbor-UCLA Medical Center, (2) University School of Medicine, Southern Illinois

Background/aims:
Milk of overweight/obese women has increased fat/calorie content, which promotes excess infant weight gain and the risk of childhood obesity. We have limited knowledge of the mechanisms contributing to high-fat milk in overweight/obese women. During lactation, the mammary gland becomes highly sensitive to insulin, resulting in upregulation of lipogenic transcription factor (SREBP) and triglyceride uptake enzymes lipoprotein lipase (LPL) and fatty acid synthase (FAS). We utilized a 3-D human mammary epithelial cell (MEC) culture to examine the effects of exogenous insulin and metformin on lipid synthesis.

Methods:
MECs were cultured on cell inserts separating a basolateral chamber containing “serum” from an apical chamber representing “milk” production. After lactogenic induction, MECs were treated with insulin (0, 2, 5 ng/ml) with and without metformin (5 µmol/L). After 48h, MECs were analyzed for protein expression of lipid factors and “milk” analyzed for secreted triglyceride. Treated vs. untreated MECs were compared by ANOVA with Dunnett’s post-hoc test. N=4 independent cultures.

Results:
In response to 2.5 and 5 ng/ml insulin, MECs demonstrated activation of lipid synthesis pathways as evident by increased expression of SREBP1 (2.3, 4.1-fold), LPL (2.2, 2.6-fold) and FAS (5.1, 7.1-fold). MEC “milk” demonstrated a dose-dependent increase in secreted triglyceride (13, 15 µM/µl). Metformin treatment normalized the insulin-induced upregulation of MEC lipid synthesis.

Conclusions:
In overweight/obese women, increased serum insulin levels may potentiate the production of high fat milk.
Consistent with effects in breast cancer cells, metformin appears to inhibit MEC insulin/insulin receptor axis-mediated activation. These findings suggest that breast milk lipid content may be normalized by maternal diet or pharmacologic interventions which reduce serum insulin or receptor activation. This culture model can be used to understand and optimize milk synthesis and composition and potentially pave the way for personalized infant nutrition.

Funding:
Fogarty NICHD Grant R01HD099813 and NIH R21HD104028

Key-words: (up to 5):
Obesity, high-fat/high-calorie milk, lactational programming

Resumen #00005527 en

Time-Course Analysis of Early Exposure to High-Sucrose Diet on MASLD Development in Male Rats.

Impact of Early Life Exposures and Environmental Pollutants

Castro Santos de Oliveira Lúcia (1), Eduardo Lopes de Macedo Bruno (1), do Carmo Silva Ribeiro Rafael (1), Késsia Corrêa Rodrigues Nathalia (1), Marinho Melo Thamys (1), Araujo Serra Pinto Bruno (1), Martins França Lucas (1), de Fátima Carvalho Brito Camila (1), Marcus de Andrade Paes Antonio (1)
(1) Department of Physiological Sciences, Federal University of Maranhão, Brazil.

Background/aims:
Excessive intake of added sugars is closely associated with metabolic syndrome and metabolic dysfunction-associated steatotic liver disease (MASLD). Although fructose-induced hepatic lipogenesis is well established, the effects of excessive sucrose intake on intestinal fructose handling and its contribution to MASLD onset remain unclear. This study investigates how early exposure to high sucrose intake modulates liver metabolism and contributes to the onset and progression of MASLD.

Methods:
Weaned male rats were fed either a regular chow (CTR, 10% sucrose) or a high-sucrose diet (HSD, 25% sucrose) for 30, 60, or 90 days (n=6–8/diet/time). At each time point, animals were euthanized for collection of blood, small intestine, liver, and adipose tissue fat pads, which were processed for further analysis (CEUA/UFMA 23115.016737/2024-38).

Results:
After 30 days of exposure, HSD rats exhibited small intestine shortening (-12.1%, $p<0.01$) along with liver function impairment, characterized by hypertriglyceridemia (+110.1%, $p<0.001$), increased TyG index (+8.9%, $p<0.001$), and elevated ALT (+37.0%, $p<0.05$) and AST (+42.2%, $p<0.05$) levels. At 60 days, in addition to the progression of these alterations and the emergence of hyperglycemia (+11.1%, $p<0.01$), HSD rats also displayed increased body weight (+6.2%, $p<0.05$), liver mass (+6.1%, $p<0.05$), and enlargement of retroperitoneal (+34.5%, $p<0.001$), mesenteric (+18.6%, $p<0.001$), and periepididymal (+33%, $p<0.001$) fat pads. Extending exposure to 90 days further worsened all the aforementioned parameters. Ongoing preliminary small intestine and liver morphology data, and gene expression analyses suggest that hepatic metabolic dysfunction precedes the onset of systemic alterations.

Conclusions:
These preliminary findings support the small intestine and liver as early targets of sucrose-induced metabolic dysfunction, highlighting a time-dependent progression toward MASLD development and subsequent systemic impairments.

Funding:
CNPq, CAPES, FAPEMA

Key-words: (up to 5):
Added sugars; enterohepatic axis; lipid metabolism; NAFLD.

Resumen #00005782 en

Challenging the dogma: post-weaning weight gain without disruption of gut microbiota in the small litters rats

Role of Infant and Young Child Feeding Practices on Long-Term Health

Rezende Ribeiro de Abreu Aline (1), Martins Silva Ana Flávia (1), Neves Freitas Nicolly (1), Jesus de Deus Isabela (1), Martins de Andrade Fagundes Miliane (2), Rosse Izinara (3), Ângelo Gonçalves de Moraes Lauro (4), Silveira Breguez Gustavo (1), Bearzoti Eduardo (5), Dutra Medeiros Julliane (6), Ariston de Carvalho Azevedo Vasco (7), Góes Neto Aristóteles (8), Guerra de Sá Renata (9), Barbosa de Queiroz Karina (2)

(1) Postgraduate Program in Health and Nutrition, Federal University of Ouro Preto, (2) Department of Food, Federal University of Ouro Preto, (3) Department of Pharmacy, Federal University of Ouro Preto, (4) Research Center in Biological Sciences/NUPEB, Federal University of Ouro Preto , (5) Department of Statistic, Federal University of Ouro Preto, (6) Department of Biology, Federal University of Juiz de Fora, (7) Department of Biological Genetic, Federal University of Minas Gerais, (8) Department of Microbiology, Federal University of Minas Gerais, (9) Department of Biological Science, Federal University of Ouro Preto

Background/aims:

The DOHaD concept highlights that early-life nutrition experiences can program long-term metabolic outcomes. Breastfeeding plays a crucial role shaping the gut microbiota, which produces short-chain fatty acids (SCFA) — key microbial metabolites essential for host metabolism regulation. Small litter size (SL) models, often linked to overnutrition during lactation, have been used to study early metabolic disruptions. However, particularly on gut microbiota development, remains to be understood. This study evaluated how SL affects gut microbiota diversity, Firmicutes/Bacteroidetes ratio and production of SCFA post-weaning.

Methods:

Eleven male Wistar rats were divided into control litter (CL, 8 pups/dam, n=5) and small litter (SL, 4 pups/dam, n=6) groups. After weaning (21 days), animals were weighed and euthanized. Cecal content was collected for 16S rRNA sequencing and SCFA analysis. Gut microbiota evaluation used QIIME2, and other data were analyzed by unpaired t-test ($P<0.05$). Approved by CEUA/UFOP (nº 2245040518).

Results:

The SL group had significantly greater weight gain ($p<0.001$) compared to the CL. No significant differences were observed in alpha diversity ($P>0.05$) but beta diversity analysis showed significant differences in species composition between groups ($P<0.019$). LEfSe analysis revealed a differential abundance of Staphylococcus sp. in SL and Enterobacter sp. in CL. However, SCFA analysis (acetate, propionate, and butyrate), total SCFA, and Firmicutes/Bacteroidetes ratio showed no significant differences ($P>0,05$).

Conclusions:

The SL group showed increased weight gain without disruption of gut microbiota composition. However, the lack of significant changes in SCFA levels, alpha diversity, and the Firmicutes/Bacteroidetes ratio raises doubts about the idea

that early overnutrition from SL increases metabolic risk. These findings imply that early experiences like SL may not be as harmful as previously believed, highlighting the need for further research on their long-term metabolic effects.

Funding:
CAPES 001, FAPEMIG APQ-02200-21, APQ-04983-22, BDP-00094-22, RED00132-16, APQ-02511-22, FINEP e UFOP.

Key-words: (up to 5):
small litter size, gut microbiota, microbiota diversity, DOHaD, short-chain fatty acids

Resumen #00005667 en

Gestational hypoxia alters the vascular aging landscape in the thoracic aorta of guinea pigs

Impact of Early Life Exposures and Environmental Pollutants

Paz Adolfo (1), Navarrete Álvaro (2), Carreño Josefa (1), Cornejo Damaris (1), Moreno Renato (1), Herrera Pedro (1), Jimenez Tamara (1), Beñaldo Felipe (1), Herrera Emilio (1) (1)
Universidad de Chile, (2) Universidad de Santiago de Chile

Background/aims:
Gestational hypoxia (GH) increases cardiovascular disease susceptibility during adulthood, associated to endothelial dysfunction and vascular remodeling, mechanisms closely related to vascular aging. We proposed that GH induces an accelerated vascular aging phenotype in the thoracic aortas of guinea pigs.

Methods:
All procedures were approved by the Bioethical Committee (20354-MED-UCH). Pregnant guinea pigs were exposed to either normoxia (720 torr, Nx) or hypoxia (470 torr, Hx) from gestational day 30 until term (~70 days). Fetal aortic blood flow velocities—maximum (Vmax) and mean (Vmean)—were assessed via ultrasound during gestation. After birth, the Hx litter returned to normoxic conditions. Newborns (one-postnatal day; n=6 per group) and adults (one-postnatal year; n=12 per group) were euthanized, and their aortas were dissected. Vasoreactivity was evaluated using wire myography (K^+-induced contraction, sodium nitroprusside [SNP] for endothelium-independent relaxation, and methacholine for endothelium-dependent relaxation). Biomechanical properties—opening angle and elastic modulus—were assessed using ring-opening and axial stress tests. Structural composition (elastin and collagen) was evaluated by histology, and vascular aging markers (P53, IL-1β, and MCP-1) were analyzed by immunohistochemistry. Data was analyzed by Two-Way ANOVA ($p \leq 0.05$).

Results:
In the fetus, GH increased the aortic Vmax during gestation compared to the normoxic counterpart. In the neonate, GH reduced SNP sensitivity, methacholine maximal response, as well as the total diameter of the vessel. Aging reduced contractile capacity as elastin tortuosity index, and increased endothelial-dependent vasodilation in Nx; while GH reverted these effects. Furthermore, in both groups the luminal and total diameters increased, and elastin tortuosity index was reduced; however, Nx exhibited an increase in luminal area and collagen deposition, along with a decrease in the intima-media area. Importantly, the opening angle increased exclusively in the Hx group during aging.

Conclusions:
GH disrupts vascular development, inducing altered aging and persistent structural and functional aortic impairments from fetal to adult stages.

Funding:
Doctoral Fellowship ANID 21230893, supported by FONDECYT Regular 1241502.

Key-words: (up to 5):
Cardiovascular aging, Endothelial dysfunction, Fetal growth restriction, Intrauterine hypoxia, Vascular senescence.

Resumen #00005732 en

Role of mHealth intervention in improving physical activity during pregnancy

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Mohammed Nuruddin (1), Vadsaria Khadija (2), Nuruddin Rozina (2), Azam Iqbal (2), Sayani Saleem (3) (1) Aga Khan University Hospital, (2) Aga Khan University, (3) Aga Khan Development Network

Background/aims:
Physical activity (PA) during pregnancy is crucial for improving maternal and fetal health outcomes. Despite its benefits, PA typically declines as pregnancy progresses. mHealth interventions have proven effective in promoting PA, however, evidence from Pakistan is scarce. This study assessed the effect of an mHealth application versus standard face-to-face counselling in improving the PA status of pregnant women.

Methods:
A randomized controlled trial implemented at Aga Khan University Hospital, involved 306 pregnant women. Participants were adults, in their first trimester, and owned smartphones. The intervention group received counselling through the PurUmeed Aaghaz mHealth app developed for the study, which provided personalized recommendations tailored to the PA history, and push messages three times a week. The non-intervention group received face-to-face counselling sessions on each contact at 6, 12, 18, and 24 weeks after enrollment. Data were collected through a structured questionnaire, and PA was assessed based on engagement in light, moderate, and vigorous activities over the past week. PA duration was measured in metabolic equivalent of task (MET) hours/week, categorized into light (1.5–2.9 METs), moderate (3–5.9 METs), and vigorous (≥6 METs) activities. Linear regression analysis was performed using Stata v.14.

Results:
After 24 weeks, both groups showed improvements in light and moderate PA engagement. The intervention group demonstrated a greater improvement in light PA (+13.7% vs. 7.9%), while the non-intervention group had a higher engagement in moderate PA (+6.4% vs. 14.9%). Multivariable analysis revealed significantly higher MET-hours/week for light (β:26.11, 95% CI:21.50–30.73) and moderate (β:25.59, 95% CI:17.19–34.03) activities in the intervention group compared to the non-intervention group.

Conclusions:
The mHealth intervention effectively supported pregnant women in maintaining PA throughout pregnancy. These findings suggest that mHealth applications can be a viable tool for sustaining PA among pregnant women, offering an alternative to traditional face-to-face counselling.

Funding:
Funding for this study was received from the University Research Council of Aga Khan University.

Key-words: (up to 5):
light, moderate, metabolic equivalent of tasks, physical activity, pregnancy

Resumen #00005659 en

Does Diabetes Fuel Cancer Risk in Mothers and Offspring? Insights from Oncogene Expression in Pancreatic Islets in an Intergenerational Experimental Model

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Paula Verônyca Gonçalves (1), Gomes Maria Eduarda Picolo (2), Gallego Franciane Quintanilha (2), Barco Vinicius Soares (2), Souza Maysa Rocha de (2), Carvalho Marcio de (2), Reis Patrícia Pintor dos (2), Damasceno Débora Cristina (2)
(1) São Paulo State University - UNESP, (2) Sao Paulo State University (UNESP)

Background/aims:
According to the DOHaD concept, changes in the intrauterine environment, such as hyperglycemia, can program the development of chronic diseases in offspring in the long term. Maternal diabetes induces epigenetic changes in glucose metabolism-sensitive tissues like the endocrine pancreas, activating pro-tumor pathways. This study aimed to investigate the expression of tumorigenesis-related genes in the pancreatic islets from diabetic rats and adult offspring of diabetic rats. The model allows the evaluation of inherited or programmed molecular modifications in a tissue that is key to metabolic homeostasis and frequently involved in neoplastic processes.

Methods:
All procedures were approved by the Animal Use Ethics Committee (#1444/2023). Diabetic female rats (Dm, n=3), female offspring of diabetic rats (ODm, n=3), and non-diabetic female rats (Control, n=3) were used, based on statistical analysis for sample size and literature. At 120 days of age (adulthood), the animals were anesthetized and the pancreases were collected to isolate pancreatic islets. RNA was extracted from the pancreatic islets and subsequently, the global gene expression was evaluated by the microarray technique. TAC, Shinygo, and KEGG platforms were used to analyze differentially expressed genes and functional enrichment analysis. For all comparisons, $p<0.05$ was statistically considered.

Results:
The pathway enrichment analysis showed overexpression of HER/2neu, KRAS, β-catenin, and BRAF oncogenes in pancreatic islets from diabetic rats and offspring of diabetic rats. The most enriched pathways included MAPK/ERK, PI3-AKT, pancreatic cancer, endometrial cancer, and colorectal cancer. Overexpression of classical tumor suppressor genes, such as TP53, BRCA1, p16, SMAD2, SMAD4, and BAX, was also observed.

Conclusions:
Diabetes and intrauterine exposure to maternal hyperglycemic environment appear to be related to epigenetic activation of pathways involved in cell proliferation and cancer, pointing to a possible intergenerational mechanism of predisposition to the disease as a consequence of hyperglycemia.

Funding:
PROPG/PROPe (05/2022), FAPESP (Process Number 2023/04866-4 and 2024/11596-6).

Key-words: (up to 5):
Diabetes; fetal programming; cancer, gene expression, rats

Resumen #00003312 en

Optimal Gestational Weight Gain and Fetal Growth in Urban Environments: The Role of Residential Greenness

Plant and Animal Health and Its Impact on Reproductive Age Individuals and Their Offspring

Wu Yan-Ting (1), Zhang Si-Wei (2), Hao Yanhui (2), Meng Xia (3)
(1) Obstetrics and Gynecology Hospital, Fudan University, (2) Fudan University, (3) School of Public Health, Fudan University

Background/aims:
The influence of residential greenness on maternal gestational weight gain (GWG) and fetal intrauterine growth remains understudied. This study examines the impact of residential greenness on GWG and fetal intrauterine growth, assessing the mediating role of GWG.

Methods:
The research included 29,406 births in Shanghai, utilizing the Normalized Difference Vegetation Index (NDVI) to measure greenness within a 500-meter radius (NDVI-500). The analysis employed a generalized linear model to assess impacts on GWG, fetal growth, and birthweight, and a mediation analysis to explore GWG's role between greenness and fetal development.

Results:
Results indicated significant benefits were observed with increased greenness, where each 0.1 unit increase in NDVI-500 was associated with reductions of 9.4% (95% CI: 5.5%–13.2%) in the risk of head circumference undergrowth and 8.5% (95% CI: 4.8%–12.2%) in estimated fetal weight undergrowth. Additionally, each 0.1 unit increase in NDVI-500 was associated with reductions of 9.4% (95% CI: 5.1%–14.4%) and 9.2% (95% CI: 6.2%–12.0%) in the risks of inadequate and excessive GWG , respectively. Notably, total GWG mediated 17.5% of the relationship between NDVI-500 and birth weight.

Conclusions:
These findings suggest that enhancing residential greenness could be an effective public health strategy to improve pregnancy outcomes by promoting fetal growth and managing GWG, with GWG partially mediating these benefits.

Funding:
This work is supported by the National Key Research and Development Program of China (2022YFC2703500), National Natural Science Foundation of China (82171686), Clinical research program of Shanghai Municipal Health Commission (202340222)

Key-words: (up to 5):
Gestational weight gain, Residential greenness, NDVI, Fetal intrauterine growth, Birthweight

Resumen #00003467 en

Title: Impact of Childhood Adversity on Menopause Timing and Symptom Severity: A Mixed Methods Study in Soweto

Impact of Early Life Exposures and Environmental Pollutants

Matina Sostina (1)
(1) Wits University

Background/aims:
The Developmental Origins of Health and Disease (DOHaD) framework posits that early life experiences influence later health outcomes. Despite growing evidence linking childhood adversity to adult disease, its impact on reproductive ageing remains underexplored. This study investigates whether early life adversities are associated with an earlier onset of menopause and more severe menopausal symptoms among women in Soweto.

Methods:
We employed a mixed methods design. Quantitative data were obtained from a cohort of 208 Soweto women using standardised measures including the Menopause Rating Scale (MRS) and retrospective assessments of childhood adversity (e.g., parental loss, economic hardship). Regression analyses evaluated the associations between early adversity indicators and both age at final menstrual period and MRS scores. Additionally, semi-structured interviews with 25 participants provided qualitative insights into personal menopause experiences and perceptions of early life challenges.

Results:
Quantitative findings indicate that women reporting higher levels of childhood adversity experienced an earlier onset of menopause and significantly elevated MRS scores ($p<0.05$), with parental unemployment and early parental loss emerging as key predictors. Qualitative data revealed that these adversities not only accelerated reproductive ageing but also shaped women's interpretations of menopause as both a natural transition and a marker of cumulative life stress.

Conclusions:
These findings suggest that childhood adversity may contribute to an earlier and more symptomatic menopausal transition. Interventions addressing early life social determinants could improve reproductive ageing outcomes, offering new avenues for promoting women's long-term health within the DOHaD framework.

Funding:
N/A

Key-words: (up to 5):
Menopause; Childhood adversity; Reproductive ageing; Mixed methods, menopause

Resumen #00004819 en

Fighting Chemotherapy-Induced Infertility: A Natural Strategy for Ovarian Protection

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Herrero Yamila (1), Velazquez Candela (1), Neira Melanie (1), Bordaquievich Mayra (1), May Maria (2), Abramovich Dalhia (1), Scotti Leopoldina (3), Parborell Fernanda (1)
(1) Instituto de Biología y Medicina Experimental (IByME), (2) Instituto de Investigaciones Farmacológicas (ININFA-UBA-CONICET), (3) Centro de Investigaciones y Transferencia del Noroeste de la Provincia de Buenos Aires

Background/aims:
Chemotherapeutic agents such as Doxorubicin (Doxo) can severely damage the female gonad, leading to premature ovarian failure (POF). Resveratrol (Res) is a natural compound with antioxidant, antiproliferative, and anti-apoptotic properties. The aim of this study was to evaluate the effect of Res on ovarian function in a Doxo-induced POF mouse model.

Methods:
F1 mice (Balb/c x C57), 8–10 weeks old, were used. Four experimental groups were established: Control, Doxorubicin, Doxorubicin + Resveratrol 7 mg/kg, and Doxorubicin + Resveratrol 15 mg/kg (n=9/group). Animals received seven intraperitoneal injections of either Res or saline solution. Mice were sacrificed 15 days after Doxo administration (10 mg/kg). Ovaries were collected for histology, immunohistochemistry, and western blot analyses. Uterine horns were isolated for histopathological assessment. All procedures were approved by the Ethics Committee (protocol CE-007/2020). Statistical analysis was performed using ANOVA followed by Tukey's test.

Results:
Doxo significantly reduced the percentage of antral follicles and ovarian reserve (DDX4) compared to control group. Res treatment increased these parameters relative to Doxo alone ($p<0.05$). Doxo decreased the proliferation index (PCNA) in follicles, whereas Res restored it ($p<0.05$). Doxo also reduced periendothelial area (α-actin), Vascular Endothelial Growth Factor (VEGF) expression, and superoxide dismutase levels (SOD); Res administration increased all of these parameters ($p<0.05$). Doxo elevated the percentage of atretic follicles, apoptotic index, and DNA damage (γH2AX), while Res reversed these effects ($p<0.05$). Uterine tissue was also affected by Doxo and partially restored by Res.

Conclusions:
Administration of Res before and during Doxo treatment may represent a non-invasive, low-cost strategy to preserve ovarian function in women undergoing chemotherapy.

Funding:
ANPCYT, INC, CONICET, Fundación Williams, Fundación René Barón

Key-words: (up to 5):
Fertility, Chemotherapy, Ovary, Resveratrol, Doxorubicin

Resumen #00004932 en

Interactive effects of genotype with prenatal stress on epigenetic variation at birth – a multi-omic approach

Mechanisms Determining Transgenerational Effects of Health and Disease

Mulder Rosa (1), Baltramonaityte Vilte (2), Defina Serena (3), Trajanoska Katerina (3), Suderman Matthew (4), Schwarz Emanuel (5), Boks Marco (6), Walton Esther (2), Cecil Charlotte (3), Felix Janine (3)
(1) Erasmus MC, (2) University of Bath, (3) Erasmus Medical Center, (4) Bristol University, (5) Heidelberg University, (6) Amsterdam UMC

Background/aims:
In utero stress exposure has been associated with a myriad of health-related outcomes. Although DNA methylation (DNAm) has been identified as a putative mechanism underlying these associations, previous efforts did not find finding robust associations between prenatal stress and DNAm. More recent research, however, has shown that environmental factors in interaction with genetic variants are better predictors of DNAm than environmental factors or genotype alone. Here, we studied whether interactions of prenatal maternal stress with genome-wide genetic variants are associated with epigenome-wide DNAm at birth. We also tested the hypothesis that DNAm is better predicted by the interaction of genetic variants and stress than by either factor alone

Methods:
We examined 2963 mother-child pairs from the population-based Generation R Study (The Netherlands) and ALSPAC (United Kingdom), using a harmonized, comprehensive cumulative prenatal stress measure. We tested genome-wide genotype-by-prenatal stress interactions on epigenome-wide DNAm (GxEmodel), and models including only genetic variants (Gmodel) or prenatal stress (Emodel) as predictors. GxEmodel findings were followed up for pathway enrichments using Gene Ontology analyses.

Results:
We report five Bonferroni corrected ($p<1.55x10-12$) SNP-by-prenatal stress interactions on DNAm, including five unique SNPs in CHD2 and ORC5, and two unique CpGs in near CHASERR and in EPPK1. By comparison, the Gmodel yielded 691,202 SNP main effects and the Emodel identified three associations at CpGs in AHRR, GFI1, and MYO1G, which are known DNAm loci for smoking exposure. Gene Ontology analyses of suggestive ($p<5.00x10-08$) GxEmodel findings pointed to enrichment of neuronal development related pathways.

Conclusions:
Our results provide some support of interaction of prenatal stress with the child's genome on DNAm of genes related to neuronal development. Results do not confirm the notion that gene-by-environment interaction models show more associations with DNAm compared to genes or the environment studied in isolation.

Funding:
Erasmus MC, Rotterdam, Erasmus University Rotterdam; the Netherlands Organization for Health Research and Development (ZonMW); the Netherlands Organization for Scientific Research (NWO); the Dutch Ministry of Health, Welfare and Sport and the Ministry of Youth and Families; the Dutch Organization for Scientific Research (NWO 2021.042, "Snellius" www.surf.nl); the UK Medical Research Council and Wellcome (Grant ref: 217065/Z/19/Z);

University of Bristol; Sample Logistics and Genotyping Facilities at Wellcome Sanger Institute and LabCorp (Laboratory Corporation of America) using support from 23andMe; the Biotechnology and Biological Sciences Research Council (BBSRC; grant numbers BBI025751/1 and BB/I025263/1) and the Medical Research Council (MRC; grand numbers MC_UU_12013/1, MC_UU_12013/2 and MC_UU_12013/8); European Union's Horizon 2020 Research and Innovation Programme (EarlyCause, grant agreement No 848158; STAGE; STAGE has received funding from the European Union's Horizon Europe Research and Innovation Programme under grant agreement nº 101137146. UK participants in Horizon Europe Project STAGE are supported by UKRI grant numbers 10112787 (Beta Technology), 10099041 (University of Bristol) and 10109957 (Imperial College London)); European Union's HorizonEurope Research and Innovation Programme (FAMILY, grant agreement No 101057529; HappyMums, grant agreement No 101057390); the European Research Council (TEMPO; grant agreement No 101039672); LongITools (No 874739); UK Research and Innovation (UKRI) under the UK government's Horizon Europe / ERC Frontier Research Guarantee [BrainHealth, grant number EP/Y015037/1]; This research was conducted while CAMC was a Hevolution/AFAR New Investigator Awardee in Aging Biology and Geroscience Research.

Key-words: (up to 5):

Prenatal stress, gene-environment interactions, epigenetics, DNA methylation, multi-omic

Resumen #00004467 en

High-polyphenols prehispanic diet effect on maternal parameters and milk production

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Delgadillo-Puga Claudia (1), Bautista-Carbajal Claudia Janet (2), Salazar-Del Pino Claudia Paulina (3), Chávez-Flores Mariana Nayeli (4), Cruz-Martínez Yessica Rosalina (2), López-Guzmán Axel (4), Hernández-Ramírez Leonardo (4),
Torre-Villalvazo Ivan (5)
(1) Instituto Nacional de Ciencias Médicas Salvador Zubirán, (2) Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, (3) Universidad Anahúac, (4) Facultad de Química, UNAM, (5) INCMNSZ

Background/aims:
Polyphenols are plant-derived bioactive compounds known for their antioxidant, anti-inflammatory, and other protective properties. The prehispanic diet (PD), composed of traditional foods such as maize, beans, chilli, and various fruits and herbs, is naturally rich in polyphenols. This study aimed to evaluate the effects of a PD on reproductive outcomes and milk production in rats.

Methods:
All procedures were approved by the INCMNSZ Animal Experimentation Ethics Committee (2047-24-27-1). Sixteen female Wistar rats were assigned to two groups: control (CD, n=8; 267.1±14.4 g BW) and PD (n=8; 260.9±27.1 g BW). The CD followed the AIN-93 formulation, while the PD included maize, beans, chilli, and tomato. Total phenolic content (TPC) was determined. Milk production was estimated on postnatal days (PND) 6, 13, and 20. Pups were separated from dams for 4 hours, weighed before and after, and reweighed 2 hours later.

Results:
TPC were 5.4 ± 0.4 y 197±14 mg GAE/100 g DM for CD and PD, respectively. Feed intake (76 days) in the control group was 24.47 ± 9.1 g/day, while in the prehispanic group, it was 27.81 ± 11.79 g/day. The conception and fertility rates were 100%: 12.9 pups per mother and 87.5%: 13 pups per mother in the PD and CD groups, respectively. The average of female and male pups was 6:7 and 7:6 in the CD and PD, respectively. Rat weight on day 21 of gestation in the control group was 445.89±36.10 g BW, and in the prehispanic group, it was 429.07±42.10 g BW. Milk production at PND 6, 13, and 20 was 334:313, 339:359, and 440:387 mg/h in the control and prehispanic group, respectively.

Conclusions:
The prehispanic diet did not alter the fertility rate, body weight, or milk production compared to the control group.

Funding:
Departamento de Nutrición Animal, INCMNSZ

Key-words: (up to 5):
Polyphenols, prehispanic diet, milk production, fertility, conception.

Resumen #00005504 en

Maternal obesity is associated with metabolic endotoxemia and altered immune phenotype in fetal monocytes and hematopoietic progenitor cells at birth

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

López-Rivera Macarena (1), Silva-Varela Cristina (2), Wichmann-Pérez Ignacio (3), Castro-Rodríguez José Antonio (4), Plösch Torsten (5), Casanello-Toledo Paola (6)
(1) Department of Medical Technology, Universidad de Chile, (2) PhD Program in Cell Biology and Biomedicine, Universidad San Sebastián, (3) Department of Obstetrics, Pontificia Universidad Católica de Chile, (4) Department of Pediatric Pulmonology, Pontificia Universidad Católica de Chile, (5) University Medical Center Groningen, The Netherlands; University of Oldenburg, Germany, (6) Department of Neonatology, Department of Obstetrics, Pontificia Universidad Católica de Chile

Background/aims:
Maternal obesity (OB) is characterized by systemic low-grade inflammation and metabolic endotoxemia (i.e., elevated blood levels of lipopolysaccharide; LPS), which may affect fetal immune programming. Hematopoietic progenitor cells (HPCs) and monocytes develop in early embryonic stages and are found in umbilical cord blood (UCB), being a window to study the fetal immune system during intrauterine life. We aimed to evaluate the effects of maternal obesity on LPS levels in the offspring, as well as the immunophenotype, gene expression, epigenetic profile, and functional response of UCB monocytes and HPCs.

Methods:
Pregnant women with obesity (OB, n=21) and normal-weight (NW, n=21) were recruited (ethics #200920001). At delivery, maternal blood and UCB were collected to measure LPS levels (photometry). Monocytes and HPCs from UCB were immunophenotyped (flow cytometry) and subsequently isolated. Inflammatory cytokine transcript levels (monocytes, RT-qPCR), global DNA methylation (monocytes, EPIC-850K), and PPARγ methylation (monocytes/HPCs, pyrosequencing) were determined. Functional response to in vitro LPS stimulation was assessed in both monocytes and HPCs (RT-qPCR and flow cytometry).

Results:
Compared to NW, OB mother-newborn dyads had higher LPS levels ($p<0.0001$) and UCB HPCs showed a shift toward early myeloid lineage ($p<0.05$). UCB monocytes displayed elevated IL-6 and IL-1β gene expression, reduced PPARγ transcript levels ($p<0.05$), and a global DNA hypomethylation ($p<0.01$). OB-UCB monocytes and HPCs exhibited increased DNA methylation in the PPARγ gene promoter compared to NW ($p<0.05$), as well as a blunted response to LPS in vitro and lower IL-6 transcripts and protein production ($p<0.05$).

Conclusions:
The offspring of women with obesity exhibit metabolic endotoxemia, and phenotypic, epigenetic, and functional changes in their immune cells, which suggest fetal immune programming induced by maternal obesity.

Funding:
Fondecyt #1171406, #1221812 (PC); DOHaD Brain Mobility Award 2021 (ML); Pediatric PUC Grant 2021(ML, PC); SOCHED 2021-11 (ML, PC); Fondecyt #1141195 (JAC)

Key-words: (up to 5):
maternal obesity, metabolic endotoxemia, immune programming, monocytes, hematopoietic progenitor cells.

Resumen #00004538 en

Maternal inflammation as a mediator of the association between pre-pregnancy diet, and child intelligence and executive function

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Harrod Marybeth (1), England-Mason Gillian (1), Vaghef-Mehrabani Elnaz (1), Field Catherine J. (2), Forbes Laura (3), Jarma Megan (4), Giesbrecht Gerald F. (1), Letourneau Nicole (1), Murias Kara (1), Ross Kharah M. (5), Lebel Catherine (1), Dewey Deborah (1)
(1) University of Calgary, (2) University of Alberta, (3) University of Guelph, (4) Aston University, (5) Athabasca University

Background/aims:
Maternal diet prior to conception provides critical nutrients that are building blocks for fetal brain development. Diet has also been associated with maternal inflammation and BMI. This study examined if maternal C-reactive protein (CRP; a marker of inflammation) mediates the association between pre-pregnancy diet, and child intelligence and executive function (EF) in BMI-stratified groups (i.e., lower BMI<25, higher BMI>25).

Methods:
274 mother-child pairs from the APrON study participated (Ethics#: REB14-1702). Diet for the year prior to pregnancy was quantified using the Mediterranean Diet Adherence (MED) and Dietary Inflammatory Index (DII). Children participated in neurodevelopmental assessments between age 3-5. Indices from the Wechsler Preschool and Primary Scale of Intelligence – IV Canadian (WPPSI-IVCND) and Behaviour Rating Inventory of Executive Function – Preschool (BRIEF-P) were used to measure intelligence and EF. Covariate-adjusted mediation analyses investigated if third trimester maternal plasma CRP concentrations mediated the association between pre-pregnancy diet, and intelligence and EF via BMI group.

Results:
In children of mothers with higher BMI, both diet measures were indirectly associated with Visual Spatial scores through CRP (MED: path ab=-0.130, 95%CI=-0.232, -0.054; DII: path ab=-0.082, 95%CI=-0.162, -0.019). In children of mothers with lower BMI, both diet measures were indirectly associated with Full
Scale IQ (MED: path ab=-0.024, 95%CI=-0.052, -0.005; DII: path ab=-0.038, 95%CI=-0.076, -0.011) and Working Memory (MED: path ab=-0.024, 95%CI=-0.050, -0.005; DII: path ab=-0.032, 95%CI=-0.067, -0.008) through CRP.

Conclusions:
CRP is a significant mediator between pre-pregnancy diet, and child intelligence and EF. These relationships differed depending on the mother's pre-pregnancy BMI. Results suggest that maternal inflammation could be a potential biological mechanism underlying these associations.

Funding:
Alberta Innovates-Health Solutions; Canadian Institutes of Health Research: MOP-123535, HTA-472411,
PG-425614, 2024 Canadian Graduate Scholarships-Master's

Key-words: (up to 5):
Pre-pregnancy diet, intelligence, executive function, maternal inflammation, BMI

Resumen #00005016 en

Prenatal exposure to maternal immune activation with SARS-Cov-2 alters the developing human brain

Impact of Early Life Exposures and Environmental Pollutants

Sigurdardottir Julie (1), Batalle Dafnis (1), Javed Ayesha (1), Eddison Molly (1), Tournier J-Donald (2), Rutherford Mary (2), Gill Carolyn (3), Doores Katie (4), Gibbons Deena (4), Poston Lucilla (3), Edwards A.David (2), McAlonan Grainne (1)

(1) Forensic and Neurodevelopmental Sciences Department, King's College London, (2) Research Department of Early Life Imaging, King's College London, (3) Women and Children's Health Department, King's College London, (4) Peter Gorer Department of Immunobiology, King's College London

Background/aims:

Antenatal maternal immune activation (MIA) can elicit a cascade of inflammatory processes adverse to fetal brain development, potentially "priming" it towards neurodevelopmental and psychiatric conditions. The brain could therefore be an accessible "intermediate" phenotype of the path from cause to outcome. Here in human neonates, we tested the hypothesis that prenatal exposure to MIA due to SARS-Cov-2 affects neurodevelopment.

Methods:

We acquired 3T structural brain MRI from n=145 neonates (75 males) with no immediate family history of neuropsychiatric conditions at mean (sd) 41.4 (2.1) weeks postmenstrual age (Ethics # 12/LO/2017) . Likely antenatal infection was defined from maternal and neonatal blood antibody responses to SARS-CoV-2 Nucleocapsid and Spike proteins. Eighty-eight newborns designated a pandemic cohort (in utero from March 2020), 33 of whom were exposed to SARS-CoV-2 MIA antenatally, and 57 were prepandemic controls. All MRI acquisition and processing followed the developing Human Connectome Project (dHCP) pipelines. We first took a regions-of-interest approach and selected brain regions associated with neuropsychiatric outcomes. We used path regression models to evaluate the effects of maternal infection on brain volumes, adjusted for sex, age at scan and birth, the pandemic cohort effect and of maternal depressive symptoms at MRI visit. We then performed a whole-brain tensor-based morphometry (TBM) analysis with the same covariates

Results:

Volumetric analyses suggest that MIA by SARS-Cov-2 reduced volume in the right anterior temporal lobe grey-matter (GM), thalamus and amygdala (p-uncorrected <0.05). TBM revealed antenatal viral exposure was associated with constriction of the right inferior temporal gyrus GM and WM and expansions of CSF compartments (e.g. 4th ventricle, quadrigeminal and interpeduncular a cisterns), left fusiform gyrus, hypothalamus and midbrain.

Conclusions:

MIA through SARS-CoV-2 infection may have elicited changes in prenatal structural neurodevelopment and CSF circulation, potentially implicating effects on the choroid plexus, however this will require long-term follow-up to understand their clinical relevance.

Funding:

Innovative Medicines Initiatives 2 No 777394

Key-words: (up to 5):
COVID-19, MRI, MIA, CSF, brain

Resumen #00005346 en

Embryonic growth in women with inflammatory arthritis and systemic lupus erythematosus: the Rotterdam Periconceptional Cohort

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Vargas-Aguirre Tania (1), Rousian Melek (2), Willemsen Sten (3), Perez-Garcia Luis (1), Dolhain Radboud (1), Steegers-Theunissen Régine (2), Mulders Annemarie (4)
(1) Department of Rheumatology, Erasmus MC University Medical Center, Rotterdam, The Netherlands, (2) Department of Obstetrics and Gynecology, Erasmus MC University Medical Center, Rotterdam, (3) Department of Biostatistics, Erasmus MC University Medical Center, Rotterdam, The Netherlands, (4) Erasmus MC University Medical Center Rotterdam The Netherlands

Background/aims:
Autoimmune diseases, such as inflammatory arthritis (IA) and systemic lupus erythematosus (SLE), affect women during their reproductive years and increase the risk of adverse pregnancy outcomes (APOs) like fetal growth restriction (FGR) and preterm delivery (PTD). During the preconception period, both disease activity and treatment are considered contributing factors. However, the impact of these factors on embryonic growth is unclear. We hypothesized that early pregnancy development might also be impaired in women with IA and SLE. Therefore, we aimed to investigate early embryonic growth in these patients and compare it with healthy controls.

Methods:
Data were obtained from the Rotterdam Periconceptional Cohort (Predict study), an open prospective birth study in Rotterdam, the Netherlands. Three groups were selected: patients with IA (n=43), patients with SLE (n=9), and healthy controls (n=59). Three-dimensional (3D) ultrasound volumes of the gestational sac were obtained at 7, 9 and 11 weeks of gestation. Virtual Reality (VR) segmentation was used to measure crown-rump length (CRL) and embryonic volume (EV), reflecting embryonic growth. A linear mixed models analysis was performed with adjustment for potential confounders.

Results:
Compared to healthy controls, there was no significant difference in CRL in women with IA (βCRL = -0.169, 95% CI -0.355; 0.016, P=0.074) or SLE (βCRL = -0.206, 95% CI -0.564; 0.150, P=0.257). Similarly, no significant difference in EV was observed in IA (βEV = -0.070, 95% CI -0.220; 0.080, P=0.363) and SLE (βEV = -0.082, 95% CI -0.405; 0.240, P=0.616), compared to the healthy controls.

Conclusions:
This exploratory study found no significant differences in embryonic growth - measured by CRL and EV between women with IA or SLE and healthy controls. Larger studies are needed to evaluate the separate effects of autoimmune diseases and their treatments on early pregnancy development.

Funding:
None

Key-words: (up to 5):
Autoimmune diseases, Embryonic growth, Pregnancy outcome, Preconception period

Resumen #00003336 en

Prenatal IgG exposure alleviates asthma in adult offspring and correlates to an increase in lung alveolar macrophages

Mechanisms Determining Transgenerational Effects of Health and Disease

Kahhaleh Fariz (1), Alhasan Moumen (2), Barrientos Gabriela (3), Fahlbusch Fabian (4), Conrad Melanie (1)
(1) I-MIDI, Charité/ Neonatology and Pediatric Intensive Care, University of Augsburg, Germany, (2) Institute of Microbiology, Infectious Diseases and Immunology, Charité Berlin, Germany , (3) Laboratorio de Medicina Experimental, Hospital Alemán - CONICET, Buenos Aires, Argentina, (4) Neonatology and Pediatric Intensive Care, Faculty of Medicine, University of Augsburg, Germany

Background/aims:
Our lab has previously demonstrated that intranasal exposure of pregnant mice to a cow-shed-derived bacteria, Acinetobacter lwoffii, reduced the severity of asthma in their progeny. The concentrations of serum total immunoglobulin (Ig)G in the mothers and offspring were elevated at different time points in the treatment group. The aim of this study is to explore the potential effect of elevated maternal IgG levels on the severity of asthma in offspring and the underlying mechanisms.

Methods:
We established a proof of concept model in which 50 mg/kg of pooled murine IgG was intraperitoneally injected into pregnant mice on gestation days (G)12 and G18. Controls received an equivalent volume of the vehicle phosphate-buffered saline. Beginning at weaning, offspring were exposed to ovalbumin (OVA) to induce an experimental asthma phenotype. Flow cytometry was used to immunophenotype G18 fetal liver and lungs, as well as postnatal day (PN)15 and PN49 offspring bone marrow, blood and lung tissue for hematopoietic stem cells, progenitors and leukocyte subpopulations.

Results:
Prenatal IgG treatment was associated with significantly reduced asthma severity in the offspring. This effect was associated with significantly increased lung alveolar macrophage (AM) populations at steady state (PN15 and PN49), accompanied by significantly decreased blood Ly6C monocytes at PN15. Except for megakaryocyte–erythroid progenitors, the proportion of hematopoietic stem cells and progenitors in PN15 and PN49 bone marrow, and G18 fetal liver did not alter significantly.

Conclusions:
Long-term protection against asthma in adult offspring could be achieved by prenatal IgG treatment. AMs could play a pivotal role in the IgG-preventive effect against asthma.

Funding:
DAAD/DFG/ Faculty of Medicine, University of Augsburg/Hospital Alemán -CONICET

Key-words: (up to 5):
DOHaD, asthma, IgG, alveolar macrophages

POSTERS

Abstract #00003321 en

Maternal obesity alters placental dopaminergic signaling: Implications for infant neurodevelopment

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Soria-Reinoso Nicole (1), Flores-Pliego Arturo (2), Espejel-Nuñez Aurora (2), Solis-Paredes Juan Mario (3), Canul-Euan Arturo Alejandro (4), Martínez-Medina Sandra (5), Torres-Calapiz Mariana (5), Perichart-Perera Otilia (6), Estrada-Gutierrez Guadalupe (2), Camacho-Arroyo Ignacio (1)
(1) Unidad de Investigación en Reproducción Humana, INPer-Facultad de Química, UNAM, (2) INPer, Departamento de Inmunobioquímica, (3) INPer, Departamento de Investigación en Salud Reproductiva y Perinatal, (4) CEAVI-P, Instituto Nacional de Pediatría, (5) INPer, Departamento de Neurobiología del Desarrollo, (6) INPer, Coordinación de Nutrición y Bioprogramación

Background/aims:
The maternal-fetal axis plays a pivotal role in shaping early human development. Emerging evidence suggests that maternal obesity may impair this axis, particularly through disruption of placental dopaminergic signaling, with potential consequences for infant neurodevelopment.

Methods:
This study, approved by the IRB of the National Institute of Perinatology-INPer in Mexico City (2021-1-11; 2024-1-14), included 33 participants from the OBESO cohort classified by pregestational BMI (pBMI) as normal weight (n=20) or obesity (n=13). All participants provided written informed consent. Infant neurodevelopment was assessed at one month using the Bayley Scales of Infant Development, Third Edition (BSID-III); scores ≤7 in any domain were considered altered. Placental dopamine (DA) was quantified by ELISA and correlated with neurodevelopmental outcomes. A subset of representative samples (normal pBMI/normal neurodevelopment vs. obesity/altered neurodevelopment) was analyzed by Western blot to assess the expression of tyrosine hydroxylase (TH), catechol-O-methyltransferase (COMT), vesicular monoamine transporter 2 (VMAT2), and dopamine receptor D2 (DRD2).

Results:
Placental DA levels positively associated with maternal weight gain. Infants of mothers with obesity had a higher prevalence of altered neurodevelopment (25%), with expressive language and cognitive domains most affected. Within this group, infants with cognitive delays exhibited higher placental DA levels with reduced TH, VMAT2, and DRD2, alongside increased COMT expression, compared to controls.

Conclusions:
Maternal obesity is associated with altered placental dopaminergic signaling that may contribute to early disruptions in cognitive development. These findings underscore the placenta´s critical role as a mediator between maternal metabolic status and infant neurodevelopment.

Funding:

This study was supported by the Instituto Nacional de Perinatología (Grants 2021-01-11 to I.C.-A; 3300-11402-01-575-17 to G.E-G.)

Key-words: (up to 5):maternal obesity, dopaminergic system, placenta, neurodevelopment.

Abstract #00003349 en

Prenatal Stress Is Linked to Clinical Markers of Insulin Resistance in Children - Findings from a Brazilian Birth Cohort

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Oewel Thais (1), Blumrich Lukas (2), Mendes Anna Carolina (1), Fernandes Maria Teresa (2), Nascimento Thais (2),
Ferraro Alexandre (2)
(1) Faculty of Medicine of the University of São Paulo, (2) Department of Pediatrics, Faculty of Medicine of the University of São Paulo

Background/aims:
The DOHaD perspective suggests prenatal stress influences offspring metabolism. Intimate partner violence during pregnancy is a critical but understudied stressor. Prenatal modulation on early insulin resistance remains unclear. In resource-limited settings, clinically relevant and easily detectable outcomes reduce reliance on costly resources. This study investigates whether maternal stress—defined by anxiety, depression, or psychological intimate partner violence during pregnancy—is associated with an easily detectable insulin resistance marker in childhood.

Methods:
A prospective, population-based birth cohort (N=126) was followed from third trimester of pregnancy to age 10. All mothers provided written consent (Institutional committees protocols 0054/09 and 122/10). Prenatal exposures included psychological violence during pregnancy (N=46), diagnosis of anxiety (N=33) and depression (N=18) at the initial interview. The primary outcome was acanthosis nigricans (AN) as continuous variable. Generalized linear models investigated the association between prenatal stress and AN. Models were adjusted for key confounders identified through a Directed Acyclic Graph and mediation analyses explored indirect pathways.

Results:
Anxiety (β = 0.54, 95% CI: 0.07–1.01, p=0.024), intimate partner violence (β = 0.467, 95% CI: 0.04–0.898, p=0.033) and the cumulative score (β = 0.302, 95% CI: 0.06–0.544, p=0.015), were associated with higher AN scores at age 10. Mediation analysis examined child's BMI, gestational weight gain, birthweight, small-for-gestational-age status, smoking, alcohol use and breastfeeding, but no significant indirect effects were found, suggesting that the association may be due to a direct effect or unincluded mediators.

Conclusions:
This study suggests an association between prenatal stress and clinical markers of insulin resistance in offspring around age 10. The composite score indicates an additive effect of exposures, providing robust evidence for our hypothesis. No significant mediators were identified, suggesting a direct effect of prenatal stress on metabolic programming.

Funding:
CNPq nº573974 / 2008-0, FAPESP nº2021/14917-0, CNPq n°143836/2021-8

Key-words: (up to 5):
prenatal stress, insulin resistance, acanthosis nigricans, intimate partner violence, birth cohort

Abstract #00003353 en

Short-term metformin treatment attenuates metabolic dysfunctions programmed by neonatal overfeeding, but not in adulthood

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Pereira Lopes Rafael (1), Rodrigues Raposo Scarlett (1), Ferreira Barbosa Leticia (1), Vinicius Martins Marcos (1),
Sayuri Fuzishima Fernanda (1), Cezar de Freitas Mathias Paulo (1)
(1) Universidade Estadual de Maringá

Background/aims:
Our objective was to evaluate whether short-term treatment with metformin during adolescence could attenuate metabolic dysfunctions programmed by neonatal overfeeding. Additionally, we investigated whether the same intervention in adulthood would have a similar effect on metabolic programming.

Methods:
The experimental protocols followed the standards of the National Council for Animal Experimentation Control (CEUA), under numbers 3220080620 and 6943140224. Wistar rats were used, with standardized litters of 9 pups per dam in the control group (NL – normal litter) and 3 pups per dam in the overfeeding group (SL – small litter). The control groups received an intraperitoneal injection of saline (NL-C and SL-C), while the treated groups received metformin (100 mg/kg) (NL-M and SL-M) from days 35 to 42 (puberty) and from days 70 to 81 (adulthood).

Results:
Two months after the intervention, in both adulthood and adolescence, SL-C animals showed metabolic dysfunctions, being significantly heavier than NL-C animals, with greater fat accumulation and disrupted glucose homeostasis ($p<0.0001$). SL animals treated with metformin during puberty showed a significant improvement in hepatic steatosis and a significant reduction in white adipose tissue ($p<0.05$). On the other hand, metformin treatment in adulthood did not significantly reduce any of the assessed parameters.

Conclusions:
Our findings indicate, for the first time, that short-term metformin treatment during puberty can attenuate metabolic dysfunctions programmed by neonatal overnutrition. However, this intervention in adulthood was not able to reverse early metabolic programming resulting from overfeeding during lactation, highlighting the relevance of the DOHaD concept.

Funding:
CNPQ, CAPES, INSPAM, JBS, ARAUCÁRIA FOUNDATION

Key-words: (up to 5):
DOHaD, Metformin, Obesy

Abstract #00003355 en

Cultural Connectedness, Health-Related Quality of Life, and Mental and Physical among Métis Children: A Latent Class Analysis

Public Health Policies Across the Life Cycle.

Brar Simran (1), Serrano-Lomelin Jesus (1), Bartel Reagan (2), Bradburn Kelsey (2), James Ashton (2), Ahmad Mariam (2), Kima June (2), Ospina Maria (1)
(1) Queen's University, (2) Otipemisiwak Métis Government of the Métis Nation within Alberta (MNA)

Background/aims:
High levels of cultural connectedness are associated with better health outcomes among Indigenous populations. However, little is known about this association in a Métis context. This study examines the relationship between cultural connectedness and caregiver-reported health-related quality of life (HRQoL), mental, and physical health among Métis children in Alberta.

Methods:
This secondary analysis used data from the 2023 Lii Zaanfaan survey, conducted in collaboration with the Otipemisiwak Métis Government of the Métis Nation within Alberta (MNA). The study included data from caregivers of Métis children aged 2-10 years old who completed all cultural connectedness and outcome measures (i.e., KIDSCREEN-10, mental health, and physical health). Latent class analysis identified cultural connectedness classes, a multiple linear regression assessed their association with HRQoL scores, and binary logistic regression examined associations with mental and physical health outcomes. All models adjusted for age, sex, caregiver income, place of residence, physical activity, and the intergenerational impacts of colonization on families.

Results:
Data from 588 respondents were analysed. Latent class analysis identified three cultural connectedness classes: Culturally Balanced Engagement, Cultural Mentorship Focus, and Nature-Land Connection. The Culturally Balanced Engagement class served as the reference group for all analyses. Both the Cultural Mentorship Focus and Nature-Land Connection classes were significantly associated with higher HRQoL scores (B=3.8, 95%CI 1.9, 5.7; B=2.1, 95%CI .5, 3.8) and better physical health outcomes (OR=8.8, 95%CI 2.8, 28.0; OR= 12.0 95%CI 4.3, 33.2). Results from the mental health analysis were not statistically significant.

Conclusions:
Compared to Métis children in the Culturally Balanced Engagement class, those in the Culturally Balanced Engagement and Nature-Land Connection classes had higher HRQoL scores, and better physical health outcomes based on caregiver reports. Findings suggest that Métis children with stronger connections to nature, land-based activities, and cultural mentorship may experience better physical health and quality of life.

Funding:
Canadian Institutes of Health Research

Key-words: (up to 5):
Indigenous health, child health, health-related quality of life

Abstract #00003363 en

Adiposity, metabolism and cardiovascular risk in scholar children born pretern

Mechanisms Determining Transgenerational Effects of Health and Disease

Machado Daudt Beatriz (1), Maman Oldra Caroline (1), Zanuzo Késia (1), Rocha Fujita Amanda (2), Batista Schmidt Helene Eveline Cristiane (1), Grassiolli Sabrina (1)
(1) Program in Biosciences and Health. State University of Western Paraná - UNIOESTE, (2) Faculdade de Ciências Aplicadas - FCA, Universidade Estadual de Campinas - UNICAMP

Background/aims:
Preterm (PT) birth negatively impacts growth, metabolism and immune functions in first year of life, elevating the risk of obesity, diabetes and cardiovascular diseases (CVD) in adulthood. Here we evaluate whether premature birth can lead to obesity and metabolic dysfunctions in schoolchildren between 5 - 9 years of age.

Methods:
Quantitative study (ethical committee n. 1.872.666; CAAE 60942716.8.0000.0107). Were analyzed scholar children (N=40) of both sexes, in a municipality in southern Brazil. The children were divided into PT (<37 weeks of gestation) and a term (AT; >37 weeks of gestation). Adiposity parameters were the body mass index (BMI; kg/m²) and waist circumference (WC; cm), classifying to CVD risk. Systolic and diastolic blood pressure (SBP and DBP; mmHg) also were registered. Blood values of glucose, total cholesterol and triglycerides were measured. Teste t or Mann-Whitney and Spearman correlation were applied.

Results:
Were evaluated 20 AT and 20 PT, with masculine sex presented higher frequency in the AT (60%) and PT (65%) groups. The frequency of eutrophic (AT: 60% and PT: 75%), overweight (AT: 20% and PT: 20%) and obesity (AT: 20% and PT: 5%). Moreover, the CDV risk was 15% in AT and 20% in the PT group. In the AT groups SBP and WC presented a positive correlation (r=0.4469; p=0.0493) as well as BMI and WC (r=0.6703; p=0.0016). Similarly in the PT children, SBP and WC showed positive correlation (r=0.5638; p=0.0107) as well as BMI and DBP (r=0.4944; p=0.0280).

Conclusions:
At 5 – 9 years of age, school-aged children born PT did not show higher adiposity or metabolic abnormalities in relation to school-aged children born AT. However, in both groups, a positive correlation was noted between visceral adiposity and SBP.

Funding:
Araucária Foundation for Scientific and Technological Development of Paraná State (nº 16/2016).

Key-words: (up to 5):
Adiposity; Childhood Obesity; Blood Pressure;

Abstract #00003401 en

Investigating the association between nationwide COVID-19 lockdowns and developmental outcomes at Age 2: a retrospective linked cohort study in England

Big Data and Cohorts in DOHaD Research., Impact of Early Life Exposures and Environmental Pollutants

Latt Su Mon (1), McAlonan Grainne (1), Poston Lucilla (1), Downs Johnny (1)
(1) King's College London

Background/aims:
The COVID-19 pandemic led to unprecedented lockdowns, limiting access to early childhood education, social interaction and play time. This can negatively impact early childhood development. This study investigated the association between experiencing national lockdowns in early childhood and children's developmental outcomes at age two.

Methods:
A retrospective cohort study (2028-2023) was conducted using linked routine health records for maternity and birth data (Born in South London–BiSL cohort) and health visiting datasets. The primary exposure was COVID-19 lockdowns. Developmental outcomes at age 2 were assessed at the health visitor contact using the Ages and Stages Questionnaires(ASQ) scores for five developmental domains. Multivariable regression models were used to investigate the association between experiencing national lockdowns and developmental scores after adjusting for maternal socio-demographics, birth characteristics, and mother's mental health.

Results:
Among the BiSL cohort, there were 12,921 mother and 2-year-old baby dyads after applying exclusion criteria. We analysed data from 5,431 children who had a health visiting contact at 2-2.5 years old. Children who experienced all three lockdown periods had a slightly lower problem-solving domain score (adjusted mean difference -1.4, p-0.01) compared to those born after the third lockdown. Multivariable logistic regression indicated that experiencing all three lockdowns, or being 18-27 months old during the third lockdown is associated with a 46% increase in the odds of ASQ score falling below the threshold in at least one domain (aOR=1.47, p 0.05)

Conclusions:
The reduction in developmental scores in children with greatest exposure to lockdown may have modest clinical significance at this age, but prompts follow up of developmental and education outcomes in later childhood. This data linkage study, which to our knowledge is the first to combine routine individual maternal data infant and health visitor data in England, has provided valuable insights into the consequences of the COVID-19 pandemic on child development.

Funding:
The eLIXIR Born in South London project is funded by a Medical Research Council in England. SML's postdoctoral position is funded through philanthropic support from Heart of Racing LLC to the Brain Health in GEN2020 programme at King's College London and the NIHR Maudsley Biomedical Research Centre (BRC).

Key-words: (up to 5):
early life exposure, neurodevelopment, covid lockdowns

Abstract #00003410 en

Association between maternal body mass index (BMI), offspring BMI trajectory and pubertal timing: a longitudinal birth cohort study

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle, Big Data and Cohorts in DOHaD Research.

Zhou Siyu (1), Hof Michel H.P. (2), Motazedi Ehsan (1), van den Boogaard Emmy (3), Vrijkotte Tanja G.M. (1)
(1) Department of Public and Occupational Health, Amsterdam University Medical Center, (2) Department of Epidemiology and Data Science, Amsterdam University Medical Center, (3) Department of Obstetrics and gynaecology, Amsterdam University Medical Center

Background/aims:
Maternal pre-pregnancy body mass index (BMI) is associated with offspring BMI trajectories and pubertal timing, yet the critical growth periods influencing pubertal timing remain unclear. This study examines the mediation role of dynamic BMI trajectories in the relationship between maternal pre-pregnancy BMI and pubertal timing in offspring, focusing on four key developmental periods: infancy (0-1 year), toddlerhood (1-3 years), preschool (3-5 years) and prepuberty(5-8 years).

Methods:
This longitudinal analysis used data from the Amsterdam Born Children and their Development (ABCD) cohort, including 2,982 mothers with pre-pregnancy BMI records and their children with repeated BMI measurements (N = 71,304) from birth to 8 years and pubertal development scale (PDS) scores at ages 11-12 years. Ethical approval was obtained, and written informed consent was provided by all participants. Child-specific BMI trajectories were modelled using a linear mixed-effects model with natural cubic spline functions in both fixed and random effects. Associations between BMI trajectories and PDS scores were modelled using ordinal logistic regression. Maternal pre-pregnancy BMI, maternal age, ethnicity, education, smoking, diabetes, hypertension and parity were added as covariates. A Bayesian approach accounting for uncertainty in BMI estimation was employed, which simultaneously estimated the linear mixed-effects model and the ordinal logistic regression model.

Results:
Higher maternal pre-pregnancy BMI was associated with earlier pubertal timing in boys (POR[95%CI]: 1.06[1.01, 1.10]) and girls (POR[95%CI]: 1.07[1.04, 1.11]). When incorporating BMI trajectories into joint models, infancy (boys: POR[95%CI]: 1.12[1.03, 1.22]; girls: 1.11[1.02, 1.20]) and prepuberty (boys: 1.23[1.08, 1.42]; girls: 1.23[1.12, 1.38]) were found as critical windows. Preschool (POR[95%CI]: 1.55[1.22,
1.99]) was an additional window for girls.

Conclusions:
Maternal pre-pregnancy BMI is associated with offspring pubertal timing, with dynamic childhood BMI trajectories acting as important mediators. Infancy and prepuberty are key developmental windows in shaping pubertal timing in both boys and girls, highlighting the importance of optimizing early-life growth to mitigate maternal BMI effects on offspring.

Funding:
This work was financially supported by ZonMw Grant (TOP, 40-00812-98-11010).

Key-words: (up to 5):

body mass index; puberty; growth trajectory; early-life risk factors

Abstract #00003412 en

Impacts of omega-3 fatty acids on pregnant mice and offspring in a pre-eclampsia model

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Matias-Silva Camila (1), Lemos Rodrigues Isabela Lúcia (1), Silva Gueiz Juliana (1), Medeiros Chagas Marya Eduarda (1), Teixeira Vogas Raíssa (1), Fernandes-Santos Caroline (1), Amorim de Morais Nascimento Braga Fernanda (2), Lonzetti Bargut Thereza Cristina (1)
(1) Fluminense Federal University (UFF), Nova Friburgo Health Institute, (2) Federal University of Rio de Janeiro (UFRJ)

Background/aims:
Preeclampsia (PE) is a multisystem pregnancy syndrome with limited treatment options, highlighting the need for new preventive strategies. This study investigated the effects of maternal fish oil (FO) supplementation on gestational and offspring outcomes in an experimental PE model.

Methods:
The protocol was approved (CEUA/UFF n° 1087190924). Female C57BL/6 mice were divided into 4 groups: control (C), PE, PE + FO1 [1.5:1 EPA/DHA], and PE + FO2 [1:5 EPA/DHA]. After mating, animals received AIN93G diets, with FO1 and FO2 groups receiving 3% of total calories from FO during gestation and lactation. PE was induced from gestational day (GD) 11 to GD21 via daily subcutaneous L-NAME (50 mg/kg). Mothers and offspring were monitored until postnatal day 90 (PND90).

Results:
Regarding the PE group, we observed that mothers had a body mass (BM) gain similar to that of the C group throughout gestation. However, there was a greater loss of offspring. In male offspring, the PE model promoted a reduction in naso-anal length (NAL) and an increase in left ventricular weight. Mothers in the FO1 group had a loss of offspring similar to the C group. Meanwhile, male offspring of this group had a reduction in BM and NAL. FO1 also restored left ventricular mass and increased brown adipose tissue weight in males. In females, there was a reduction in CNA. Regarding FO2, mothers presented elevated loss of pups until weaning. In these female offspring, a reduction in the glycemic response was observed after 60 and 120 min of glucose overload.

Conclusions:
The PE model promoted deleterious changes that were partially attenuated by the use of FO, which also promoted other beneficial effects. This indicates a possible protective role for these fatty acids, although the data are controversial, and further studies are needed.

Funding:
Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brazil (CAPES), Doctoral Scholarship; Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ), scientific initiation scholarship.

Key-words: (up to 5):
Pre-Eclampsia; Fish Oils; Fatty Acids, Omega-3; Metabolic Reprogramming; Pregnancy outcomes

Abstract #00003419 en

Lower ambient temperatures around conception are associated with improved metabolic outcomes in adulthood

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle, Effects of Environmental Climate Change on Early Life Health Setting in Future Generations., Impact of Early Life Exposures and Environmental Pollutants

Münz Timo (1), Pradella Fabienne (2), Lambrecht Nathalie (3), Gabrysch Sabine (4), Van Ewijk Reyn (1)
(1) Johannes Gutenberg University Mainz, (2) Johannes Gutenberg University Mainz / Heidelberg University / Stanford University, (3) Charité Berlin / Potsdam Institute for Climate Impact Research / Stanford University, (4) Potsdam Institute for Climate Impact Research / Heidelberg University / Charité Berlin

Background/aims:
Environmental factors around conception can play a crucial role in epigenetic programming, thereby shaping an individual's health trajectory from the earliest stages of development. Animal studies and correlational evidence from human studies suggest that pre-conception cold exposure increases the amount of active brown fat in adulthood, resulting in better metabolic outcomes. However, causal evidence on humans is lacking.

Methods:
We use a large-scale dataset from the UK Biobank with 430,000 individuals born between 1934 and 1971, and integrate historical temperature data to examine the link between ambient temperature around conception and later metabolic health. To isolate the impact of temperature on metabolic health, we utilize day-specific temperature deviations during the pre-conception period relative to the long-term mean temperature for the same location and day of the year. With this approach, we leverage the quasi-random nature of temperature variations.

Results:
Our results indicate that individuals who were conceived when temperatures were lower than usual have a lower body mass index (BMI), smaller waist circumference, and lower levels of triglycerides and total cholesterol in adulthood. We find no evidence for an effect on glycated hemoglobin (HbA1c).

Conclusions:
These findings show that the basis for metabolic health in adulthood may be partly laid in the first stages of development, i.e., around conception. More generally, these results demonstrate that environmental factors such as ambient temperatures can have long-term health effects in humans.

Funding:
This research was funded by the German Research Foundation (DFG grant 455841434).

Key-words: (up to 5):
Cold Temperatures, Metabolic Health, Preconception, Climate Change Impacts, Brown Fat

Abstract #00003420 en

Is it a Match? Cognitive Development in Response to Prenatal and Postnatal Drought-Related Nutritional Challenges

Impact of Early Life Exposures and Environmental Pollutants , Effects of Environmental Climate Change on Early Life Health Setting in Future Generations., Big Data and Cohorts in DOHaD Research.

Pradella Fabienne (1), Gabrysch sabine.gabrysch@uni-heidelberg.de (2), Van Ewijk Reyn (3)
(1) Johannes Gutenberg University Mainz / Heidelberg University / Stanford University, (2) Potsdam Institute for Climate Impact Research / Heidelberg University / Charité Berlin, (3) Johannes Gutenberg University Mainz

Background/aims:
Poor maternal nutrition during pregnancy is associated with adverse health and human capital outcomes in the offspring over their life courses, yet the role of the postnatal environment for effect manifestation remains understudied. We investigate the interplay of pre- and postnatal drought-related nutritional shocks in shaping cognitive health among adolescents in rural India.

Methods:
Math and reading scores from the 2007-2018 Annual Status of Education Report (ASER) on
11-16-year-olds from rural India (N = 2,009,869) were linked to University of Delaware rainfall data. Rural India heavily depends on rainfed agriculture, so that rainfall variation proxies for nutritional shocks in a quasi-experimental set-up. Drought was defined as rainfall below the 20th percentile of the district-specific long-term mean. We analyzed the interaction effect between prenatal drought exposure with drought exposure in childhood, while adjusting for, sex, age, year of assessment and district fixed effects.

Results:
Drought exposure during pregnancy was associated with lower test scores in adolescence (reading, math, total score). Notably, children who experienced droughts in their second third life years were better prepared for drought circumstances if they had already been exposed to a drought prenatally, as indicated by positive interaction terms between prenatal and postnatal exposure. Effects did not differ by sex.

Conclusions:
Prenatal exposure to suboptimal nutrition might prepare the developing organism to deal with similar shocks in early postnatal life, with positive impacts on cognitive performance years later. This finding is in accordance with epigenetic theories predicting that prenatal conditions sensitize developing organisms for similar postnatal circumstances.

Funding:
This research was funded by the German Research Foundation (DFG grant 455841434).

Key-words: (up to 5):
Rainfall variation, Predictive Adaptive Responses, developmental plasticity, cognitive health, prenatal nutrition

Abstract #00003432 en

Intrauterine growth restriction induces increased astrocytic and neuronal O-glycosylation in hypothalamic nuclei of adult offspring.

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Alves de Sena Fourniol Jéssica (1), Tanaka Tânia Leiko (1), Andrade Iracema Sena (1), Pedroso Amanda (1), Mutran Thaís Antônio José (1), Araújo Diana Dias (1), da Silva Neto Artur Francisco (1), Oyama Lila Missae (1), Ribeiro Eliane Beraldi (1), Telles Monica Marques (1)
(1) Federal University of São Paulo

Background/aims:
Intrauterine growth restriction(IUGR) is associated with the development of obesity, hypothalamic alterations, and impaired glucose metabolism. The O-glycosylation with N-acetylglucosamine(O-GlcNAc) of proteins is glucose-dependent and may influence energy balance in the hypothalamus. This study aimed to evaluate the density of O-GlcNAc-modified proteins and their colocalization with neuronal(NeuN) and astrocytic(GFAP) markers in the arcuate(ARC), lateral(LH) and ventromedial(VMH) hypothalamic nuclei of IUGR animals.

Methods:
During gestation, female Wistar rats on caloric restriction(RG) received 50% of the food intake of control rats(CG). At 90 days old, male pups(n=3/group) were anesthetized,perfused with PBS and paraformaldehyde, and decapitated for brain collection. The brains were frozen at -80°C and sectioned into 30µm coronal sections using a cryostat, then stored at -20°C in an antifreeze solution until immunofluorescence processing. Sections were incubated overnight with primary antibodies(anti-O-GlcNAc,anti-NeuN, and anti-GFAP)and for 2 hours with fluorescent secondary antibodies(AlexaFluor568,AlexaFluor488). They were then mounted on slides and imaged with a confocal microscope. Fluorescence signals were quantified with Image J software. Statistical analysis was performed using Student's t-test. UNIFESP Animal Use Ethics Committee:nº1115260121

Results:
The RG group showed higher colocalization of O-GlcNAc with the astrocytic marker GFAP in the ARC and VMH($p<0.001$),as well as reduced astrocyte labeling($p\leq0.05$). In the LH, higher colocalization of O-GlcNAc with the neuronal marker NEUN($p=0.01$)and O-GlcNAc labeling($p<0.05$) were observed in RG. Reduction in NEUN labeling was observed in both the ARC and LH($p<0.01$).

Conclusions:
The increased neuronal and astrocytic O-glycosylation induced by IUGR in specific hypothalamic nuclei related to energy balance, along with the reduced labeling of these important functional cells,suggests changes in cellular signaling that may compromise hypothalamic homeostatic mechanisms and contribute to obesity.Present data suggest that O-GlcNAc could be one of the mechanisms involved in the relationship between IUGR and the development of late obesity in offspring.

Funding:
São Paulo Research Foundation (FAPESP, Brazil, grant number:#2020/11985-1) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPQ, Brazil).

Key-words: (up to 5):
Fetal programming; balance energy;hypothalamus; O-GlcNAc; maternal malnutrition.

Abstract #00003434 en

Offspring adiposity and energy balance is affected by paternal cholic-acid feeding in a mouse model

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Schoonejans Josca (1), Pataia Vanessa (2), Papacleovoulou Georgia (2), Nikolova Vanya (2), Williamson Catherine (1) (1) Imperial College London, (2) King's College London

Background/aims:
We showed that paternal bile acid overload (a model of cholestasis) programmed hepatosteatosis and hypertension in male offspring, but effects on adipose tissue remain unexplored.

Methods:
Male C57BL/6 mice were fed chow diets supplemented with 0.5% cholic acid (CA), mimicking high serum bile acids (hypercholanaemia) in cholestasis. After mating with control-fed females, offspring from two independent cohorts were weaned onto normal chow (NC) until 12 weeks. After this, one male and female from each litter was challenged with a Western diet (WD) until tissue collection. In cohort 1, energy expenditure (EE) was determined via indirect calorimetry at 16 weeks, and gene expression in male offspring subcutaneous white adipose tissue (sWAT) by qRT-PCR at 18 weeks of age.

Results:
CA-feeding decreased paternal adiposity and increased litter size ($p<0.05$). Paternal hypercholanaemia decreased offspring sWAT weight ($p<0.05$, model includes both cohorts and sexes), most robustly in males and in WD-fed offspring. EE was increased in male WD-fed offspring of CA-fed fathers ($p<0.05$), but not significantly affected in females. Paternal CA-feeding decreased Cd36 expression in males irrespective of diet ($p=0.086$). Paternal hypercholanaemia also decreased Dgat1 expression in NC-fed offspring ($p<0.05$), while paternal effects on CA-WD offspring were likely masked by the strongly decreased Dgat1 in response to WD ($p<0.0001$). Offspring sWAT% inversely correlated to EE ($p<0.05$) and litter size ($p<0.05$) in all males; and positively to paternal adiposity in NC-fed males ($p<0.05$). Decreased Dgat1 expression in NC-fed offspring correlated to increased litter size ($p<0.05$) and higher energy expenditure ($p<0.01$).

Conclusions:
Paternal CA-feeding decreased subcutaneous adiposity in adult offspring irrespective of offspring diet, which in males may be related to higher energy expenditure (via Dgat1) and reduced fatty acid uptake (via Cd36). Data from NC-fed offspring suggest decreased paternal adiposity and increased litter size may underlie programming effects of paternal hypercholanaemia on offspring WAT.

Funding:
King’s College London, Imperial College London

Key-words: (up to 5):
paternal programming; adipose tissue; cholestasis

Abstract #00003435 en

Prenatal metformin exposure and sex-specific cardiovascular outcomes in aged offspring of obese glucose intolerant mouse pregnancy

Interventional strategies to prevent late-life outcomes resulting from early-life insults, Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Schoonejans Josca (1), Wilsmore Phoebe (2), Mennitti Lais (2), Wong Kwun (2), Ashmore Thomas (2), Garrud Tess (2), Blackmore Heather (2), Patey Olga (2), Fernandez-Twinn Denise (2), Giussani Dino (2), Ozanne Susan (2) (1) University of Cambridge, Imperial College London, (2) University of Cambridge

Background/aims:
Metformin, a common oral treatment for diabetes in pregnancy, readily crosses the placenta. However, effects of fetal metformin exposure on long-term health remain under-explored. This study investigated long-term cardiovascular effects in offspring exposed to maternal metformin treatment using a well-established mouse model of obese glucose intolerant pregnancy.

Methods:
Female mice were given chow (n=18), or a high fat high sugar diet with/without 300mg/kg/d oral metformin (n=18/18) during gestation. At 3, 6, and 12 months of age, echocardiography and tail-cuff plethysmography were performed within the same male and female offspring (n=12 per sex per group). At 12 months, tissues were collected for wire myography, histology, and molecular analyses.

Results:
Metformin exposure programmed increased adiposity in male and female offspring in an age- and sex-dependent manner. Regardless of metformin exposure, male offspring of obese dams had cardiac diastolic dysfunction from 6 months (increased E/A ratio) without changes in systolic blood pressure. Following maternal metformin treatment, male offspring showed additional signs of diastolic dysfunction (decreased deceleration time) at 12 months. They also had increased cardiac weight and collagen expression, and vascular sympathetic hyperreactivity in response to phenylephrine, suggesting the intervention worsened the cardiovascular phenotype in aged male offspring. Female offspring of obese dams had increased systolic blood pressure throughout life and femoral vasoconstrictor hyper-reactivity and aortic wall remodelling at 12 months. Metformin treatment did not improve this and caused obesity-induced systolic hypertension at 12 months, significantly correlating to hyperleptinaemia and hyperinsulinaemia observed at this age.

Conclusions:
Maternal obesity caused sex-specific cardiovascular changes in aged offspring, with predominantly cardiac and vascular alterations in male and female offspring, respectively. Maternal metformin introduced further sex-dependent cardiovascular alterations, worsening the phenotype. Long-term cardiovascular offspring follow up of both sexes from human pregnancies treated with metformin is crucial.

Funding:
British Heart Foundation; Medical Research Council; Wellcome Trust

Key-words: (up to 5):
maternal obesity; hypertension; diastolic dysfunction; metformin; cardiovascular

Abstract #00003444 en

DIFFERENTIAL EFFECTS OF PATERNAL AND MATERNAL ULTRA-PROCESSED FOODS INTAKE ON NEONATAL ANTHROPOMETRY.

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Sartorelli Daniela (1), Carvalho Mariana Rinaldi (1), Santos Izabela da Silva (1), Baroni Naiara Franco (1), Carreira Natália Posses (1), de Lima Maria Carolina (1), Miranda Daniela Elias Goulart de Andrade (2) (1) Ribeirão Preto Medical School, University of Sao Paulo, (2) University of Ribeirao Preto

Background/aims:
Background/aim: Studies investigating the effect of paternal consumption of ultra-processed foods (UPF) on birth weight are warranted. The aim of this study was to investigate the effect of the energy percentage (%E) of UPF in the parental diet on birth weight and neonatal anthropometry.

Methods:
Methods: A cohort study nested in a randomized controlled trial was conducted among adult pregnant women with overweight (BMI 25.0-29.9 kg/m2). For this analysis, only the mother-neonate (n=135) and father-neonate (n=45) binomials of the control group were considered. The %E of UPF in the parental diet was estimated using 24-hour dietary recalls adjusted by the Multiple Source Method. Parental and neonatal anthropometric data were assessed. Adjusted linear regression models were used to investigate the effect of the %E of UPF consumption of the pregnant women and fathers, separately, on neonatal anthropometry. Directed acyclic graphs were used to select the covariables. The study was approved by the Research Ethics Committee (97288818.0.0000.5414 and 96680318.5.0000.5414), and all human welfare and ethical considerations have been met.

Results:
Results: The median (P25, P75) %E of UPF from maternal and paternal diet was 25 (18, 32) and 25 (21, 39), respectively. Adjusted linear regression models showed that the %E of UPF of the maternal diet in early pregnancy was inversely related to birth weight [β - 17.2 (-26.72; - 7.74), p<0.001] and birth length [β - 0.057 (-0.100; -0.013), p=0.011]. On the other hand, the %E of UPF of the paternal diet was directly associated with birth weight [β 12.66 (2.85; 22.46), p=0.013], supra-iliac skinfolds [β 0.025 (0.006; 0.045), p=0.012] and thigh skinfolds of the neonate [β 0.036 (0.006; 0.065), p=0.022].

Conclusions:
Conclusion: The data suggest differential effects of maternal and paternal UPF consumption on neonatal anthropometry.

Funding:
Funding: FAPESP (2021/06586-3;2021/06486-9;2017/15386-2;2021/06468-0), CNPq (302959/2021-1;406000/2018-2), CAPES (001), FAEPA (1039/2018;1114/2018;61/2019;62/2019;754/2021).

Key-words: (up to 5):
Key-words: Ultra-processed foods, POHaD, Neonatal anthropometry

Abstract #00003469 en

: Impact of Childhood Adversity on Menopause Timing and Symptom Severity: A Mixed Methods Study in Soweto

Impact of Early Life Exposures and Environmental Pollutants

Matina Sostina (1)
(1) Wits University

Background/aims:
The Developmental Origins of Health and Disease (DOHaD) framework posits that early life experiences influence later health outcomes. Despite growing evidence linking childhood adversity to adult disease, its impact on reproductive ageing remains underexplored. This study investigates whether early life adversities are associated with an earlier onset of menopause and more severe menopausal symptoms among women in Soweto

Methods:
We employed a mixed methods design. Quantitative data were obtained from a cohort of 208 Soweto women using standardised measures including the Menopause Rating Scale (MRS) and retrospective assessments of childhood adversity (e.g., parental loss, economic hardship). Regression analyses evaluated the associations between early adversity indicators and both age at final menstrual period and MRS scores. Additionally, semi-structured interviews with 25 participants provided qualitative insights into personal menopause experiences and perceptions of early life challenges.

Results:
Quantitative findings indicate that women reporting higher levels of childhood adversity experienced an earlier onset of menopause and significantly elevated MRS scores ($p<0.05$), with parental unemployment and early parental loss emerging as key predictors. Qualitative data revealed that these adversities not only accelerated reproductive ageing but also shaped women's interpretations of menopause as both a natural transition and a marker of cumulative life stress.

Conclusions:
These findings suggest that childhood adversity may contribute to an earlier and more symptomatic menopausal transition. Interventions addressing early life social determinants could improve reproductive ageing outcomes, offering new avenues for promoting women's long-term health within the DOHaD framework

Funding:
N/A

Key-words: (up to 5):
Menopause; Childhood adversity; Reproductive ageing; Mixed methods, menopause

Abstract #00003483 en

Placental miRNAs and the AMPK/GLUT pathway: association with maternal and neonatal metabolism in birthweight alterations

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Valente-Godinez Hector-Alfredo (1), Rodríguez Nemry (2), Lopez-Olmos Karina (1), Barbosa-Sabanero Gloria (1), Kaeffer Bertrand (3), Bolaños-Jimenez Francisco (4), Lazo-de-la Vega-Monroy Maria-Luisa (1)
(1) Medical Sciences Department, Health Sciences Division, University of Guanajuato Leon Campus, (2) Medical Sciences Department, Health Sciences Division, University of Guanajuato Leon CampuS, (3) Nantes Université, INRAE, UMR 1280, Physiologie des Adaptations Nutritionnelles, (4) Nantes Université, INRAE, UMR 1280, Physiologie des Adaptations Nutritionnelles,

Background/aims:
Birth weight is a marker of metabolic adult health, influenced by placental function. AMPK and GLUT1 play crucial roles in placental physiology. However, AMPK/GLUT1 regulation and interrelation in human placenta remains under study. We aimed to analyze the expression of the AMPK/GLUT1 pathway and its regulation by specific miRNAs in placentas of newborns with idiopathic birth weight alterations.

Methods:
A cross-sectional study was performed on 60 placentas from term newborns: 18 SGA (small for gestational age), 18 AGA (appropriate for gestational age), 5 LGA (large for gestational age) from healthy mothers; and 9 LGA-OB (LGA from mothers with obesity). Maternal and newborn's clinical and biochemical data were obtained from medical records. AMPK and GLUT1 gene and protein expression were assessed by RT-qPCR and western blot. miR-148b-3p and miR-33b-5p were evaluated by RT-qPCR. The study was approved by the corresponding committees (HGL-GTSSA002101-337, CIBIUG-P36-2022).

Results:
AMPK (PRKAA1) mRNA expression was higher in the LGA-OB group compared to AGA, SGA, and LGA groups, but no differences in GLUT1 (SLC2A1) were found. AMPK protein expression and activation (p-AMPK), along with GLUT1, were higher in SGA compared to LGA. AMPK expression and activation correlated with GLUT1 protein levels. miR-33b-5p was higher in the LGA group compared to AGA and LGA-OB, while miR-148b-3p was lower in SGA and LGA compared to AGA. AMPK activation correlated with maternal glucose levels. miR-148b-3p correlated with maternal triglycerides and neonatal glucose.
However, miRNA expression did not correlate with AMPK/GLUT1 expression.

Conclusions:
Our results suggest GLUT1 and AMPK are interrelated in human placenta, responding to maternal metabolism and influencing fetal growth. AMPK/GLUT1 pathway may be regulated by mechanisms beyond the evaluated miRNAs. Our findings enhance the understanding of placental function and fetal development, evidencing potential targets to improve long-term health.

Funding:
VGHA: CONAHCyT fellowship (CVU:831938). DAIP-UG (CIIC 139/2021).

Key-words: (up to 5):
Placenta, miRNAs, AMPK, GLUT1, birthweight

Abstract #00003574 en

Maternal B12 deficiency during pregnancy dysregulates fatty acid metabolism and induces inflammation in human adipose tissue

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

BOACHIE JOSEPH (1) (1)
University of Cape Coast

Background/aims:
Adipose tissue (AT) responds to excess calorie intake, however, the deficit in micronutrients accompanied by the modern lifestyle is often overlooked. Micronutrient deficiency in pregnancy, particularly vitamin B12 (B12) is commonly associated with higher adiposity, dyslipidaemia and type2diabetes. Studies have demonstrated that dyslipidaemia can trigger pro-inflammatory status. However, the release of the pro-inflammatory factors in a tissue-specific micronutrient deficient environment is unexplored. Therefore, we investigated the role of B12 deficiency on lipid metabolism and inflammatory mediators in both in vitro and ex vivo models including human pre-adipocytes, primary adipocytes, mature human white AT (WAT) and its association with metabolic risk.

Methods:
Paired abdominal subcutaneous and omental WAT (ScWAT & OmWAT) were chosen based on serum B12 (<150pM) from 115 Caucasian pregnant women. Human primary Sc-adipocytes from women with different BMI (lean, overweight, obese, morbidly obese) and pre-adipocyte cell line (Chub-S7) were differentiated in various concentrations of B12. Serum B12, folate, lipids, cytokines, biochemical parameters, gene expression, intracellular TG and mitochondrial dysfunction were assessed.

Results:
In pregnant women with low B12 levels, BMI and serum TG were significantly higher, and HDL was lower ($p<0.05$). B12 deficiency in both depots of AT correlated with higher expression of genes in FA synthesis, elongation, desaturation, TG synthesis and reduced fatty acid oxidation (FAO) ($p<0.05$). In vitro adipocytes with low B12 demonstrated that TG synthesis utilizing radiolabelled-FA was higher and mitochondrial function was impaired. We also found that the expression of pro-inflammatory cytokines in AT was increased, and circulatory cytokines inversely associated with B12 ($p<0.05$).

Conclusions:
Our novel data highlights that B12 deficiency dysregulates lipids and induces inflammation in AT and circulation, which could contribute to adipocyte dysfunction exacerbating cardio-metabolic risk during pregnancy.

Funding:
The present study received funding from sponsors: Sir Jules Thorn Charitable Trust, UK; Medical Research Council, UK; QR fund, Nottingham Trent University, UK; and the Open Access Fund from the Nottingham Trent University

Key-words: (up to 5):
Vitamin B12, Adipose tissue, Low grade inflammation, Lipid metabolism, Obesity, Pregnancy

Abstract #00003575 en

Metformin inefficiency to lower lipids in vitamin B12 deficient HepG2 cells is alleviated via Adiponectin-AMPK axis

Mechanisms Determining Transgenerational Effects of Health and Disease

BOACHIE JOSEPH (1) (1)
University of Cape Coast

Background/aims:
Prolonged metformin treatment decreases vitamin B12 (B12)-levels, whereas low B12 is associated with dyslipidaemia. Some studies have reported that metformin has no effect on intrahepatic triglyceride (TG) levels. Although AMPK activation by adiponectin lowers hepatic TG content, its role during B12 deficiency and metformin is not explored. We investigated whether low B12 impairs the beneficial effect of metformin on hepatic lipid metabolism via the AMPK-adiponectin axis

Methods:
HepG2 was cultured using custom-made B12 deficient Eagle's Minimal Essential Medium (EMEM) in different B12-media concentrations, followed by 24-hour metformin/adiponectin treatment. Genes and proteins expressions, total intracellular TG, radiochemical analysis of TG synthesis and seahorse mitochondria stress assay were undertaken.

Results:
In low B12, total intracellular TG and synthesized radiolabelled TG were increased. Regulators of lipogenesis, cholesterol and genes regulating fatty acid (FA), TG and cholesterol biosynthesis were increased. FA oxidation (FAO) and mitochondrial function were decreased, with decreased pAMPKα and pACC levels. Following metformin treatment in hepatocytes with low B12, gene and protein expression of above targets were not alleviated. However, in presence of adiponectin, intrahepatic lipid levels in low B12 decreased via upregulated pAMPKα and pACC levels. Again, combined adiponectin and metformin treatment ameliorated the low B12 effect and resulted in increased pAMPKα and pACC, with subsequent reduction in lipogenesis, increased FAO and mitochondria function.

Conclusions:
Adiponectin co-administration with metformin induced a higher intrahepatic lipid-lowering effect. Overall, we emphasize the potential therapeutic implications for hepatic AMPK activation via adiponectin for a clinical condition associated with B12 deficiency and metformin treatment

Funding:
University of Warwick Chancellors scholarship; Ghana Education Trust Fund (GETFUND)

Key-words: (up to 5):
Lipid metabolism; non-alcoholic fatty liver disease (NAFLD); fatty acid oxidation (FAO); mitochondria; obesity

Abstract #00003618 en

Mental Health Programming: Influences of Placental Iron Homeostasis and Prenatal Stress

Mechanisms Determining Transgenerational Effects of Health and Disease

Furrer Timothée (1), Schröder Mariana (1), Albrecht Christiane (1)
(1) University of Bern

Background/aims:
Gestational stress (GS) is a known risk factor for later-life mental health disorders in the offspring. Additionally, iron deficiency, one of the most common conditions during pregnancy, might contribute to this effect, since iron has essential roles in monoamine synthesis, myelination, and brain development. Considering this, we aimed to investigate 1) how GS affects placental iron homeostasis in mice, and 2) the long-term consequences of impaired placental iron balance on adult mouse offspring behavior.

Methods:
To study the effects of stress on placental iron metabolism, we implemented a chronic GS protocol on wild-type mice. Next, to explore whether abnormal placental iron metabolism directly affects fetal programming of mental health, we selectively knocked-down (KD)/knocked-out (KO) the placental intracellular iron transporter divalent metal transporter 1 (DMT-1/Slc11a2) using the placenta specific Cyp19 Cre-line. Adult mouse offspring were then subjected to a battery of behavioral tests to assess depression-like and anxiety-like behaviors, memory, and activity levels. All animal welfare considerations were met (BE112023 and BE232023).

Results:
GS increased placental iron uptake via transferrin receptor 1 (TfR1) and low-density lipoprotein receptor-related protein 1 (LRP-1), leading to iron accumulation in the placenta, specifically in females. DMT-1 KO animals showed high mortality in the early stages of gestation. Among the heterozygous mice, only males showed the expected reduction in placental DMT-1, which resulted in long-term anxiety-like and depression-like behaviors.

Conclusions:
Our findings suggest that GS significantly influences placental iron regulation, particularly in female offspring. Notably, DMT-1 appears to play a critical role in embryonic development, as homozygosity for DMT-1 resulted in lethality. Additionally, DMT-1 knockdown may impair placental iron transport and contribute to long-term mental health outcomes in a sex-dependent manner. Together, these findings highlight altered placental iron metabolism as a key driver of long-term mental health.

Funding:
NCCR-TransCure (51NF40-185544), Lindenhof Foundation (17-15-F).

Key-words: (up to 5):
Programming, Mental health, Prenatal stress, Placental iron homeostasis

Abstract #00003622 en

Prenatal exposure to per- and polyfluoroalkyl substances (PFAS) and epigenetic age acceleration in infants

Impact of Early Life Exposures and Environmental Pollutants

England-Mason Gillian (1), Reardon Anthony J.F. (2), Merrill Sarah M. (3), MacDonald Amy M. (4), Kinniburgh David W. (4), Giesbrecht Gerald F. (5), Letourneau Nicole (5), Martin Jonathan W. (6), Kobor Michael S. (7), Dewey Deborah (5)
(1) Health Canada / University of Calgary, (2) Health Canada / University of Alberta, (3) University of Massachusetts Lowell , (4) Alberta Centre for Toxicology, (5) University of Calgary, (6) Stockholm University, (7) University of British Columbia

Background/aims:
Epigenetic modifications may be one mechanism underlying associations between prenatal exposure to per- and polyfluoroalkyl substances (PFAS) and child health and development. However, limited research has examined epigenetic biomarkers such as epigenetic age acceleration (EAA). Our objective was to examine the associations between prenatal exposure to PFAS and infant EAA.

Methods:
This study included 149 maternal-infant pairs from the Canadian APrON cohort. Maternal-infant pairs (51% female infants) were included if mothers provided second trimester blood samples and 3-month-old infants provided buffy coat blood samples. Concentrations of twelve PFAS, including linear and branched isomers, were quantified in maternal plasma and the Horvath pan-tissue epigenetic clock estimated EAA in infant peripheral blood. Robust regressions examined covariate-adjusted associations between log2-transformed PFAS and EAA in the overall sample and sex-stratified groups. Bayesian kernel machine regressions examined chemical mixture effects.

Results:
Geometric means of PFAS ranged from 0.03 (PFDoA) to 2.40 ng/mL (linear-PFOS). Many analytes were moderately to highly correlated (rho > 0.50). Adjusted robust regressions showed that higher prenatal concentrations of perfluoroalkyl sulfonate isomers were associated with increased EAA in the overall sample (linear-PFOS: B=0.06, 95%CI=0.01,0.11; ∑3m-+4m-PFOS: B=0.06, 95%CI=0.01,0.11; 5m-PFOS: B=0.05, 95%CI=0.01,0.10; iso-PFOS: B=0.05, 95%CI=0.01,0.10). Specifically, for each doubling in these analytes, there was a 0.05 to 0.06 year (i.e., approximately 18 to 22 day) increase in biological age in 3-month-old infants. Sex-specific associations were found for some perfluoroalkyl sulfonate isomers. Chemical mixture models provided evidence of non-linear associations and that perfluoroalkyl sulfonates and carboxylates may have opposite direction effects on EAA.

Conclusions:
Prenatal PFAS exposures may influence infant epigenetic aging rates, potentially in a compound-specific and sex-specific manner. These findings warrant replication in other pregnancy cohorts with larger sample sizes.

Funding:
CIHR(MOP-123535;PG-425614;HTA-472411), NIH(1R21ES021295-01R21)

Key-words: (up to 5)

Per- and polyfluoroalkyl substances (PFAS); Epigenetic clock; Mixtures analysis; Perfluoroalkyl carboxylates; Perfluoroalkyl sulfonates

Abstract #00003625 en

Cultural Connectedness and Health-Related Quality of Life and Other Well-Being Outcomes among Indigenous Populations in CANZUS Countries: A Systematic Review

Public Health Policies Across the Life Cycle.

Brar Simran (1), Ospina Maria B (1), Ben Albert (1)
(1) Queen's University

Background/aims:
Cultural connectedness–the extent to which individuals feel connected to their culture through practices, language, traditions, and identity– is increasingly recognized as a key determinant of health among Indigenous peoples across the life course. High levels of cultural connectedness are associated with improved health-related quality of life (HRQoL). Although several studies have explored this relationship, the evidence has not been comprehensively synthesized in systematic reviews.

Methods:
A comprehensive search of six databases was conducted on June 10th, 2024, to identify observational studies examining the association between cultural connectedness and HRQoL, mental health or physical health among Indigenous populations in Australia, Canada, New Zealand, and the United States. Two independent reviewers conducted screening, data extraction and risk of bias assessment. Risk of bias assessments were assessed using the Newcastle-Ottawa Scale for cohort studies and its adapted version for cross-sectional studies. An effect direction plot and vote counting were used for data synthesis.

Results:
From 6,533 records, 13 studies met the inclusion criteria (Canada n=3; Australia n=1; New Zealand n=3; United States n=6). They evaluated the association between cultural connectedness and HRQoL (n=2), mental health (n=9) and physical health (n=4). Study populations included babies (n=1), youth (n=2), adults (n=8), and elders (n=2). HRQoL studies reported a positive association with cultural connectedness. Seven studies found greater cultural connectedness was associated with better mental health outcomes. Studies reporting negative associations showed non-significant p-values. All studies on physical health found positive associations.

Conclusions:
In countries with similar histories of colonialism, Indigenous people with greater cultural connectedness consistently reported better HRQoL, mental health, and physical health across different age groups. These findings highlight the importance of cultural identity and continuity as protective factors and support the integration of culturally grounded approaches in Indigenous health strategies across the life course.

Funding:

Key-words: (up to 5):
Cultural connectedness, Indigenous research, health-related quality of life

Abstract #00003654 en

Mechanistic insights into metabolic signatures of adiposity in early childhood from the Brazilian National Survey on Child Nutrition (ENANI-2019)

Mechanisms Determining Transgenerational Effects of Health and Disease

da Silva Rosa Freire Samary (1), Nahuel Keller Victor (1), Machado Schincaglia Raquel (2), de Freitas-Costa Nathalia Cristina (1), Normando Paula (1), Rugani Ribeiro de Castro Inês (3), Rodrigues Driele (1), Goldenberg Lucas (1), de Paiva Lopes Oliveira Mirella (2), Kroezen Zachary (4), Shanmuganathan Meera (4), Britz- McKibbin Philip (4), Kac
Gilberto (1)
(1) Federal University of Rio de Janeiro, (2) Federal University of Goias, (3) State University of Rio de Janeiro, (4) McMaster University

Background/aims:
New advances in metabolomics may offer biochemical insights into the developmental origins of health and disease risk in early childhood. This study investigated the association between the serum metabolome and BMI z-score (BMI-z) in a national survey of Brazilian children aged 6-59 months.

Methods:
Untargeted metabolomic data from 5,004 serum samples from the Brazilian National Survey on Child Nutrition comprised seventy-five polar/ionic metabolites and was performed using multisegmented injection-capillary electrophoresis-mass spectrometry. The BMI-z score in children was defined according to the WHO standards. Partial least square regression and linear regression models were performed, and a sex-stratified analysis was also conducted. The confounding variables were identified using a Diagram Acyclic Graph, which included birth weight, preterm birth, per capita family income, food diversity, food security, child development, age, and breastfeeding status. Benjamini–Hochberg correction adjusted p-values <0.05 were considered statistically significant. Approved by the ethics committee; all participants gave informed consent (CAAE 89798718.7.0000.5257).

Results:
The serum metabolites tyrosine (β=0.09), aminooctanoic acid (β=0.09), valine (β=0.08), lysine (β=0.07), threonine (β=0.06), deoxycarnitine (β=0.06), leucine (β=0.06), creatinine (β=0.06), phenylalanine (β=0.05), carnitine (β=0.05), methionine (β=0.05) showed a direct association with BMI-z, and proline betaine (β=-0.05) showed an inverse association with BMI-z. After sex-stratification, serum deoxycarnitine (β=0.10), creatinine (β=0.09), and threonine (β=0.08) were directly associated only for boys, while phenylalanine (β=0.09) only for girls.

Conclusions:
The results revealed a significant association between a child's BMI-z and specific serum metabolites that may increase fat storage and risk for insulin resistance. Some of those metabolites are essential amino acids, which depend on diet and are influenced by family income, parental education, and food security.

Funding:
CAPES, MS, and MCTIC

Key-words: (up to 5):
metabolome; malnutrition; infant growth.

Abstract #00003658 en

Maternal Adverse Childhood Experiences (ACEs) as a predictor of child neurodevelopmental outcomes

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Harrod Marybeth (1), England-Mason Gillian (1), Letourneau Nicole (1), Giesbrecht Gerald F. (1), Dewey Deborah (1) (1) University of Calgary

Background/aims:
Maternal adverse childhood experiences (ACEs) have been associated with developmental outcomes in young children, such as poorer fine motor skills and more behaviour and executive function problems. However, there is limited research examining the association between maternal ACEs and children's intelligence. This study aimed to examine: 1) the associations between maternal ACEs and intelligence, motor, behavioural, and executive function outcomes in children aged 3 – 5, and 2) whether associations were child sex-specific.

Methods:
334 mother-child pairs from the APrON cohort participated (Ethics#: REB14-1702). Mothers completed the ACEs questionnaire at study intake in the first or second trimester of pregnancy. Children participated in a neurodevelopmental assessment between 3 and 5 years of age; Full Scale IQ score from the Wechsler Preschool and Primary Scale of Intelligence – IV Canadian (WPPSI-IVCND) assessed intelligence; Movement Assessment Battery for Children 2 (M-ABC 2) total score assessed motor skills; inhibitory self-control, flexibility, and emergent metacognition indices from the Behaviour Rating Inventory of Executive Function – Preschool (BRIEF-P) assessed executive functions; internalizing and externalizing problems scores from Child Behaviour Checklist (CBCL) assessed behaviour. Covariate-adjusted robust regressions examined the associations between maternal ACEs and children's neurodevelopmental outcomes. Sex-stratified associations were explored.

Results:
In the overall sample, there were no significant associations between maternal ACEs and any neurodevelopmental outcomes. However, sex-specific analyses revealed that maternal ACEs were positively associated with internalizing problems in girls (B=0.18; 95%CI=0.05, 0.31). In boys, there were no significant associations observed.

Conclusions:
This study revealed that higher maternal ACEs were associated with more internalizing problems in girls only. This may indicate that future research aimed at reducing the intergenerational transmission of risk should explore child sex-specific intervention strategies.

Funding:
Alberta Innovates-Health Solutions; Canadian Institutes of Health Research: MOP-123535, PG-425614, HTA-472411, 2024 Canadian Graduate Scholarships-Master's, ACHRI: One Child Every Child Alliance
Against Violence and Adversity Student Stipend

Key-words: (up to 5):
Maternal ACES, preschool children, internalizing problems, neurodevelopmental outcomes, sex-specific effects

Abstract #00003665 en

Comprehensive Analysis of Open Chromatin Regions in the Liver of a Mouse Model of Prenatal Undernutrition: Investigation of Transcriptional Regulation

Mechanisms Determining Transgenerational Effects of Health and Disease

Itoh Hiroaki (1), Mizuno Yuri (1), Nakabayashi Kazuhiko (2), Kawai Tomoko (2)
(1) Hamamatsu University School of Medicine, (2) National Center for Child Health and Development

Background/aims:
Prenatal undernutrition is known to increase the risk of developing metabolic syndrome later in life. In this study, we used a mouse model to examine how prenatal undernutrition affects subsequent gene expression regulation in the liver.

Methods:
Pregnant C57BL/6 mice were divided into an ad libitum feeding group and a restricted feeding group (60% of the caloric intake of the ad libitum group) from embryonic day 11.5 until birth. After birth, caloric intake was equalized through nursing by foster mothers, and from postnatal week 9, the offspring were fed a high-fat diet (60% fat content). From week 17, the mice continued on the high-fat diet and were further divided into a group receiving secondary bile acid (Tauroursodeoxycholic acid; TUDCA) and a vehicle control group. At postnatal weeks 9, 17, and 22, liver tissue was subjected to ATAC-seq (Assay for Transposase-Accessible Chromatin) to comprehensively identify open chromatin regions.

Results:
Prenatal undernutrition significantly exacerbated hepatic steatosis induced by high-fat diet consumption at week 17. TUDCA treatment significantly ameliorated hepatic steatosis at week 22. Database analysis revealed that transcription factor X was most frequently bound to the regions that were open prior to high-fat diet consumption (week 9) and the regions that closed after five weeks of TUDCA treatment compared to the vehicle group (week 22). Transcription factor X has been reported to play a crucial role in the regulation of hepatic steatosis. We are currently investigating the function of transcription factor X in the liver under conditions of prenatal undernutrition and TUDCA treatment.

Conclusions:
Our findings suggest that transcription factor X may play a critical role in the accumulation of hepatic fat due to prenatal undernutrition and subsequent high-fat diet consumption, as well as in the ameliorative effects of TUDCA treatment.

Funding:
This study was supported by Japan Society for the Promotion of Science KAKENHI Grant Numbers JP23K09544, JP22K15917, JP20K16886, JP20H03823, JP24K02585, AMED under Grant Number JP20gm1310009 and SRF.

Key-words: (up to 5):
DOHaD, fetal undernutrition, hepatic steatosis, NAFLD, MASLD

Abstract #00003666 en

Impact of the Covid-19 pandemic on cancer mortality in Brazil and its environmental implications: a temporal analysis

Public Health Policies Across the Life Cycle.

Almeida Iasmim Gonçalves (1), Leão-Cordeiro Jacqueline Andréia Bernardes (2), Bariani Emanuely Magalhães Melo Borges (3), Bariani Leandro Cancellara de Oliveira (3), Felix Juliana Paula (4), Oliveira Marcus Vinícius Paiva de (1), Ataídes Fábio Silvestre (1), Vilanova-Costa Cesar Augusto Sam Tiago (5), Silva Antonio Marcio Teodoro Cordeiro (6)
(1) Medical School, School of Medical and Life Sciences, Pontifical Catholic University of Goiás, (2) Faculty of Nursing, Federal University of Goiás, (3) Honcord, (4) Polytechnic and Arts School, Pontifical Catholic University of Goiás, (5) Araújo Jorge Cancer Hospital, Association for Cancer Combat in Goiás, (6) Graduate Program in Environmental and Health Sciences, Pontifical Catholic University of Goiás

Background/aims:
Cancer mortality is influenced by environmental factors, healthcare access, and crises like Covid-19. The pandemic disrupted healthcare services, potentially delaying diagnoses and worsening prognoses. Additionally, pollution and climate variations impact cancer incidence and mortality. This study analyzes cancer mortality trends in Brazil, focusing on Covid-19 and environmental determinants.

Methods:
A time-series study was conducted using mortality data (1979-2023) from the Brazilian Mortality Information System (DATASUS). Causes of death were classified using ICD-9 (1979-1995) and ICD-10 (1996-2023). Statistical analyses in RStudio included linear regression and the Mann-Kendall test to evaluate trends. The impact of Covid-19 (2020-2023) was assessed using standardized mortality ratios (SMR) with 95% confidence intervals, based on Poisson distribution. Expected deaths were estimated with an ARIMA model. Environmental factors, including pollution and climate variations, were examined for regional disparities. As the data used in this study are secondary and publicly accessible, according to the Open Data Policy of the Federal Government of Brazil, submission to a Research Ethics Committee was not required.

Results:
Cancer mortality exhibited a significant increasing trend over 45 years. During 2020-2021, excess deaths were observed overall; however, cancer-related mortality decreased, likely due to Covid-19 disproportionately affecting cancer patients. The ARIMA model provided reliable mortality predictions, with residual autocorrelation assessed by the Ljung-Box test. Regional disparities in cancer mortality suggest a possible influence of environmental factors, such as air pollution and climate variations.

Conclusions:
Cancer mortality in Brazil continues to rise, with regional disparities possibly linked to environmental factors. The Covid-19 pandemic indirectly influenced cancer mortality by increasing overall deaths while reducing cancer-specific mortality. These findings highlight the need for an integrated health approach that considers pollution and climate change. These insights emphasize the interconnection between human, environmental, and healthcare factors. Future research should explore causal pathways and targeted interventions.

Funding:

No external funding was received.

Key-words: (up to 5):

Cancer mortality, time-series analysis, Covid-19 impact, environmental health, One Health.

Abstract #00003668 en

Impact of Gestational Diabetes Mellitus on the Human Milk Microbiome and the Early Intestinal Microbiota of Infants

Role of Infant and Young Child Feeding Practices on Long-Term Health

Zhou Xiaobo (1), Wang Andi (1), Zhang Hua (1)
(1) The First Affiliated Hospital of Chongqing Medical University, Chongqing, China

Background/aims:
Breast milk provides essential nutrients and bioactive compounds critical for neonatal immune development. It also contains the human milk microbiome (HMM), which supports maternal mammary health and seeds the infant gut, shaping early microbial colonization and immune maturation. While gestational diabetes mellitus (GDM) is known to disrupt maternal metabolism, its effects on the HMM and subsequent neonatal gut microbiota remain poorly understood.

Methods:
In this prospective cohort study in southwestern China, we recruited 50 normoglycemic and 42 GDM-diagnosed mothers. Within seven days postpartum, colostrum was collected and transferred into sterile polypropylene tubes. Concurrently, meconium specimens were obtained from predominantly breastfed neonates within the first week of life, capturing freshly meconium within 15 minutes into sterile tubes. All participants provided written informed consent (No. 2020-567). Microbial profiles were assessed using Illumina MiSeq PE300.

Results:
Both cohorts' breast milk microbiomes were dominated by Firmicutes, Proteobacteria, Bacteroidetes, and Actinobacteria (>96% of sequences). However, GDM milk exhibited a significant compositional shift: Firmicutes decreased from 57.7% to 31.1%, and Bacteroidetes from 10.7% to 5.5%, whereas Proteobacteria increased from 24.7% to 57.5% and Actinobacteria from 3.1% to 4.2%. At the genus level, GDM samples were enriched in Achromobacter (48.9% vs. 10.8%) and depleted in Pedobacter, Streptococcus, and Staphylococcus compared with controls. Neonatal meconium from the GDM group showed elevated Veillonella (14.6% vs. 2.7%) and Klebsiella (9.8% vs. 3.4%), with slight increases in Enterococcus, Clostridium, and Enterobacter, and reductions in Staphylococcus and Streptococcus. LEfSe analysis (LDA ≥ 3) identified one phylum, seven families, and twelve genera significantly enriched in the GDM cohort.

Conclusions:
GDM associated alterations in the milk microbiome correlate with distinct patterns of early gut colonization in neonates, suggesting potential long term implications for immune development and disease risk.

Funding:
National Natural Science Foundation of China (No. 82271715) and the 111 Project (Yuwaizhuan [2016] 32).

Key-words: (up to 5):
Gestational Diabetes Mellitus; Human Milk Microbiome; Infant Gut Microbiota

Abstract #00003672 en

Parental adverse childhood experiences and telomere length in offspring at birth and at 5-years old – results from The FinnBrain Birth Cohort Study

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Klimek Magdalena (1), Karlsson Hasse (2), Karlsson Linnea (2), Perasto Laura (2), Vitikainen Emma I.K. (3), Hasempour Niloofar (2), Lukkarinen Minna (2), Lund Rikka (2), Tuulari Jetro J. (2), Paunio Tiina (3), Kataja Eeva-Leena
(4)
(1) Jagiellonian University, Krakow, Poland, (2) Turku University Hospital and University of Turku, Turku, Finland, (3) University of Helsinki, Helsinki, Finland, (4) University of Turku and Turku University Hospital, Turku, Finland

Background/aims:
Emerging evidence shows that parental early postnatal years are yet another crucial time window of programming effects that can be a major contributor to the offspring's later-life trajectories. One of the most meaningful factors shaping the early environment is the exposure to adverse childhood experiences (ACEs). Previous research has suggested that health risks associated with ACEs could cascade over generations as a form of intergenerational transmission. One of the potential consequences of this transmission could be accelerated cellular aging in the offspring. Here, we explore the association between parental ACEs and offspring cellular aging expressed via leukocyte telomere length (LTL).

Methods:
Data were collected among 1134 maternal-paternal-child triads as part of the FinnBrain Birth Cohort Study. Parental ACEs were assessed by the Trauma and Distress Scale (TADS) at gestational week 12. A blood sample was collected among the offspring at the time of birth and after 5 years to estimate the LTL. General linear models and mixed-effects linear models were performed with several potential confounders. The study was approved by the Ethics Committee of the Hospital District of Southwest Finland.

Results:
Maternal ACEs, experienced between 0-6 and 7-12 years of age, were negatively related to offspring's LTL at age 5 (p=.011; p=.026, respectively). Additionally, when sex-specific analyses were performed, negative associations between selected maternal TADS scores and offspring's LTL were observed, yet only in boys at birth (p=.023) and at 5 years old (p-values ranged between .003-.029). No significant associations were detected when paternal ACEs were explored.

Conclusions:
This is a novel and preliminary study suggesting the potential intergenerational effect of maternal ACEs on offspring's LTL. We also present the first exploration of potential intergenerational effects of paternal ACEs on offspring LTL. Future studies are crucial to evaluate if cellular aging processes are also determined via intergenerational continuity.

Funding:
This study was funded by the Academy of Finland #308589, The Centre for Excellence, Finnish research
Council, #346121, Signe and Ane Gyllenberg Foundation, Finnish State Grants for Clinical Research (VTR), Finnish Cultural Foundation, Yrjö Jahnsson Foundation, and Emil Aaltonen Foundation. The study was also financially supported by the Jagiellonian University International Relations Office within the Erasmus+ program and "Better research for better quality of life – qLIFE" program (qL.1.4.2024.7).

Key-words: (up to 5):
Cellular aging, childhood maltreatment, early-life stress, intergenerational transmission

Abstract #00003696 en

BMI during childhood and puberty- associations with blood pressure

Big Data and Cohorts in DOHaD Research.

Lilja Lina (1), Bygdell Maria (1), Martikainen Jari (1), Li Huiqi (1), Schmidt Caroline (1), Bergström Göran (1),
Rosengren Annika (1), Ohlsson Claes (1), Kindblom Jenny (1)
(1) Gothenburg University

Background/aims:
A high BMI in adults is strongly associated with increased blood pressure. However, the relative contribution of an elevated BMI during childhood and puberty to blood pressure in midlife is not clear. We aimed to evaluate the association between BMI during childhood and puberty and blood pressure in midlife, and to explore midlife BMI as a potential mediator of these associations.

Methods:
We linked the BMI Epidemiology Study Gothenburg (BEST) with developmental BMI, to the Swedish CArdioPulmonary bioImage Study (SCAPIS) with blood pressure and hypertension in midlife (n=2394). The associations between childhood BMI (7-8 years) and pubertal BMI change (young adult BMI minus childhood BMI) and blood pressure and hypertension in midlife, were evaluated using linear or logistic regression models. Mediation analysis was conducted to evaluate the indirect effect, via midlife BMI, on blood pressure and hypertension. All analyses were adjusted for birth year and smoking.

Results:
The pubertal BMI change was positively associated with systolic and diastolic blood pressure and hypertension in midlife, independent of childhood BMI, in both men (systolic blood pressure: 1.45 mmHg per SD increase (95%CI, 0.40; 2.50)) and women (systolic blood pressure: 1.73 mmHg per SD increase (95%CI, 0.45;3.01). For men but not for women, childhood BMI was positively associated with systolic and diastolic blood pressure in midlife, independent of the pubertal BMI change. No significant independent association was observed for childhood BMI with hypertension. Mediation analyses for the association between the pubertal BMI change and blood pressure and hypertension in midlife revealed that these associations were largely mediated by BMI in midlife.

Conclusions:
These findings indicate that high blood pressure may originate in early life. We therefore suggest that targeted prevention during the developmental years could reduce the life-course burden associated with high blood pressure.

Funding:
This study was supported by the Swedish Research Council (J.M. Kindblom: 2021-01439; C. Ohlsson: 2020-01392; A. Rosengren: 2023-02144), the Heart-Lung Foundation (J.M. Kindblom: 2022-0406; 2022-0620; A. Rosengren: 2021-0345) and by grants from the Swedish state under the agreement between the Swedish government and the county councils, the ALF-agreement (L. Lilja ALFGBG-1002990, J.M. Kindblom: ALFGBG-965996, C. Ohlsson: ALFGBG-720331, ALFGBG-965235, and ALFGBG-965744), the Emelle Foundation (L. Lilja), The Gothenburg Society of medicine (L. Lilja GLS-999506), the Lundberg Foundation (C. Ohlsson: LU2021-0096), the Torsten Söderberg Foundation (C. Ohlsson: M65/15), the Novo Nordisk Foundation (C. Ohlsson: NNF 190C0055250 and 22OC0078421), the Knut and Alice Wallenberg

Foundation (C. Ohlsson: KAW, 2015.0317), the Swedish Society for Medical Research (M. Bygdell PD20-0012) and Region Västra Götaland, Research and Development Centre (L. Lilja).

Key-words: (up to 5):

Puberty, body mass index, blood pressure, cardiovascular disease, cohort study

Abstract #00003815 en

Uncovering Paternal Inheritance beyond DNA: Sperm miR/30ac Shapes Early Embryo and Fetal Development.

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Olatunji Oluwabunmi (1), Lyon Hannah (1), Pacella-Ince Leanne (2), Nottle Mark (1), McPherson Nicole (1) (1) University of Adelaide, (2) Repromed

Background/aims:
Paternal factors like obesity, stress, and advanced age are linked to impaired embryo development and increased fat in newborns. Though sperm-specific microRNAs (miRs) delivered at fertilisation are suspected to influence these outcomes, their causal role remains unclear. This study investigates the impact of miR/30ac, a sperm-specific miR, on embryo and fetal development.

Methods:
A mouse model was developed to overexpress sperm-specific miR/30ac using a testes-specific CCNA1-EGFP-miR/30ac construct. Zygotes were collected after mating transgenic males with superovulated females (N=6) or through natural mating (N=10/genotype). Pregnancy rates, litter sizes, and fetal/placental development were assessed at 18.5 days of gestation. Offspring metabolic health was tracked up to 16 weeks. A complementary model of depleted zygotic miR/30ac on early embryo development was also assessed. Embryos were evaluated for morphokinetics and blastocyst cell counts. All procedures were ethics-approved (#M/2023/098, #M/2021/086).

Results:
Transgenic males showed a 4-fold increase in miR/30ac ($P<0.01$) without changes in body composition or fertility. However, embryos had slower progression to the blastocyst stage, with significant delays from pronuclear fading to 2-cell and from expanded to hatching blastocyst ($P=0.0346–0.0467$). Depletion of miR/30ac in the zygote also delayed 2-cell development ($P<0.05$) and reduced blastocyst cell counts. Litter sizes and fetal weights from transgenic sires were lower ($P<0.05$, $P=0.0003$), with female offspring showing persistent lower body weights, proportion of adiposity and altered glucose metabolism at 16 weeks ($P<0.05$).

Conclusions:
Both overexpression and depletion of sperm/zygotic miR/30ac disrupt early embryo development, reduce blastocyst quality, and impair offspring growth and metabolism. This study is the first to establish a causal link between sperm miR dysregulation and fetal development, offering new insight into paternal epigenetic influence.

Funding:
Australian Research Council (ARC) Discovery Early Career Researcher Award (DECRA) DE220101449.

Key-words: (up to 5):
Paternal-inheritance, sperm-specific microRNAs, embryo and fetal development.

Abstract #00003949 en

The effect of maternal mental health during the COVID-19 pandemic on childhood health outcomes: The EPPOCH pregnancy cohort

Impact of Early Life Exposures and Environmental Pollutants

Datye Swarali (1), van Teijlingen Edwin (2), Khashu Minesh (3), Vinayakarao Latha (3), Fahlbusch Fabian (4), Conrad Melanie (1)

(1) Charite' Universitätsmedizin Berlin, Berlin, Germany and University of Augsburg, Augsburg, Germany, (2) Centre for Midwifery and Women's Health, Bournemouth University, Bournemouth, United Kingdom, (3) University Hospitals Dorset NHS Foundation Trust, Poole, United Kingdom, (4) University of Augsburg, Augsburg, Germany

Background/aims:

Prenatal maternal mental health problems are associated with a higher risk of allergies in children. The COVID-19 pandemic exacerbated mental health challenges among expectant mothers, providing a unique opportunity to examine the effects of maternal mental health on childhood health outcomes. The aim of the study was to assess the impact of the pandemic on prenatal maternal mental health and perceptions of perinatal care in the United Kingdom (UK) compared to other countries. Additionally, we investigated the association between prenatal maternal mental health and allergic manifestations such as wheezing and dermatitis in children at two years of age.

Methods:

From June-November 2020, we established a longitudinal pregnancy cohort in the UK, enrolling 3600 participants who completed validated questionnaires on mental health during the pandemic. Their children were followed up annually from birth to four years of age to monitor respiratory infections and allergic conditions.

Results:

We found elevated anxiety, pregnancy-related anxiety, depression and anger among expectant mothers during the pandemic. Prevalence of depression in the UK was 2.28 times higher than pre-pandemic levels (2012–2016) and 2–6 times higher than that reported in five other countries. Participants expressed concerns about inconsistent public health communication and restrictions on support persons in perinatal care. Maternal generalized anxiety was associated with a higher risk of atopic dermatitis, while maternal depression was linked to recurrent wheezing at two years of age. Pregnancy-related anxiety was associated with an increased likelihood of seborrheic dermatitis in children. Additionally, maternal irritable bowel syndrome was linked to atopic dermatitis and wheezing in early childhood.

Conclusions:

Our findings suggest that the pandemic led to compromised prenatal mental health in the UK and subsequently increased the risk of allergic outcomes in early childhood.

Funding:

Konrad Adenauer Foundation; European Society for Pediatric Research.

Key-words: (up to 5):

Pregnancy, Depression, Anxiety, Wheezing, Dermatitis

Abstract #00004106 en

Gut microbiota development, antibiotic resistome and related perinatal factors in early infancy: a prospective study

Impact of Early Life Exposures and Environmental Pollutants

Ouyang Fengxiu (1), Fan Pianpian (1), Ma Jinqian (2), Shen Qianwen (3), Ouyang Youcheng (4), Zhang Ting (1), Liu Zhiwei (3)

(1) Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, (2) School of Exercise and Health, Shanghai University of Sport, (3) Department of Neonatology, International Peace Maternity and Child Health Hospital, (4) School of Food Science and Engineering, Jiangxi Agricultural University

Background/aims:

Early life is a critical window for gut microbiota development and antibiotic resistomes. We aimed to investigate the microbiota longitudinal change during the first 6 months of life and difference associated with assisted reproductive technology (ART) use, mode of delivery, and infant sex.

Methods:

Gut microbiota was measured by metagenomic sequencing of faecal samples repeatedly collected within 3 days after birth, at 42 days, 3 and 6 months in 155 Chinese infants.

Results:

Among vaginal delivery, with increasing age, Ace index gradually increased from 25.4±5.2 (mean±SD) at first 3 days to 35.4±5.9 at 6 months; accordingly, relative abundance of Actinobacteria phylum increased (from 43±37% to 57±36%) and Proteobacteria phylum decreased (from 48±36% to 17±25%); and Bifidobacterium and Klebsiella genus increased and Escherichia genus decreased. The number of antibiotic resistance genes (ARGs) increased with age. The dominant ARGs was macB and msbA from first 3 days to 6 months. Infants born by cesarean section exhibited a similar yet more fluctuating trajectory in their gut microbiota. Boys and girls had similar features. Cesarean section was associated with lower Bacteroidetes phylum and lower Bacteroides genus at each age points. Compared with non-ART infants born with vaginal delivery, ART infants had higher number of phylum at age 42 days and 3 months in gut microbiota.

Conclusions:

Our findings confirmed increasing diversity and composition evolution of gut microbiota in the first 6 months of life. Both mode of delivery and ART conception are associated with early gut microbiota alteration.

Funding:

The National Natural Science Foundation of China (No. 81961128023, 81673178), Shanghai Municipal Education Commission-Gaofeng Clinical Medicine Grant (No. 20152518).

Key-words: (up to 5):

gut microbiota, early life, infants, metagenomic sequencing, prospective study, assisted reproductive technology

Abstract #00004135 en

Fetal programming by a high-fat diet promotes delay in neurodevelopmental parameters, while neonatal supplementation with 5-HTP and pyridoxine minimizes reflex delay in the offspring

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Alves-de-Sena-Fourniol Jéssica (1), Tavares Dias Clarissa (1), Santos Batista Vanessa (2), Oliveira Moraes Edicarlos (2), Barreto-Medeiros Jairza (2), Deiró Tereza Cristina Bomfim de Jesus (2), Mendes-da-Silva Cristiano (1) (1) Federal University of São Paulo, (2) Federal University of Bahia

Background/aims:
Maternal high-fat diet(HFD) harms offspring neurodevelopment,while serotonin serves as an important neurotrophic factor during the critical period.This study aimed to evaluate the effects of neonatal supplementation of the precursor of serotonin,5-HTP associated with vitaminB6 on neurodevelopmental parameters of the offspring of mothers submitted to HFD during the critical period.

Methods:
Thirty-two male Wistar rat neonates born to mothers fed a control diet(CD)or high-fat diet(HFD) during gestation and lactation received oral supplementation from postnatal day(PND) 2 to 21with 5-HTP(20 mg/kg/day)+vitaminB6(50 mg/kg/day)or saline(0.9% NaCl) forming the groups:HFD5-HTP+B6(n=10),HFDSAL(n=7),CD5-HTP+B6(n=8) and CDSAL(n=7). FromPND1 to 21,reflex maturation was assessed (palmar grasp(PG), righting(R),vibrissae placing(VP), cliff avoidance(CA),negative geotaxis(GN), auditory startle(AS),and free-fall righting(FR)). Cranial growth (laterolateral(ELLC) and anteroposterior(EAPC) axes) was measured fromPND1 to 40.Statistical Analysis:GEE for longitudinal and GzLM for cross-sectional data.Ethics approval:UNIFESP CEUAnº4600030320.

Results:
HFDSAL showed delayed maturation of VP($p<0.0001$),GN($p<0.001$) andFR($p<0.05$)reflexes vs.CDSAL while HFD5-HTP+B6 anticipated maturation of VP andFR reflexes vs.HFDSAL($p<0.05$),but delayed GN maturation vs.CD5-HTP+B6($p<0.001$).
The HFDSAL group showed greater ELLC growth fromPND14 to 40 compared to CDSAL($p<0.01$). HFD5-HTP+B6 had reduced growth vs.CD5-HTP+B6 on PND1 and 7($p<0.01$), but increased growth on PND27 and 40($p<0.05$).Compared to HFDSAL, HFD5-HTP+B6 showed reduced ELLC growth fromPND1 to 40($p<0.05$).
The HFDSAL group showed reduced EAPC vs.CDSAL on PND1($p<0.0001$) and7($p<0.01$),with no differences after PND14. HFD5-HTP+B6 had lower EAPC than CD5-HTP+B6 fromPND1 to 21($p<0.0001$) and on PND27 and40($p<0.05$),and also lower than HFDSAL fromPND14 to 27($p<0.01$).

Conclusions:
Maternal HFD altered offspring cranial structure and delayed reflex maturation.Supplementation with 5-HTP and vitaminB6 attenuated the delay of two reflexes altered by HFD,but did not minimize the alterations in cranial axes.

Funding:
Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) - Brazil

Key-words: (up to 5):
neurodevelopment; reflex ontogeny; neonatal suplementation, serotonin

Abstract #00004175 en

Multi-ancestral, trans-generational genome-wide association meta-analysis of gestational diabetes mellitus and glycaemic traits during pregnancy

Big Data and Cohorts in DOHaD Research.

Brito Nunes Caroline (1), Rukins Valentina (2), McBride Nancy (3), Cisse Aminata (4), White Frédérique (5), Moen Gunn-Helen (1), on behalf of the GENetics of Diabetes In Pregnancy (GenDiP) Consortium (6)
(1) Institute for Molecular Bioscience, The University of Queensland, (2) Estonian Genome Centre, Institute of Genomics, University of Tartu, (3) MRC Integrative Epidemiology Unit, University of Bristol, (4) Department of Clinical and Biomedical Sciences, University of Exeter, (5) Département de Biologie, Faculté des Sciences, Université de Sherbrooke, (6) GENetics of Diabetes In Pregnancy (GenDiP) Consortium

Background/aims:
During pregnancy, changes in maternal glucose metabolism are essential to meet maternal and fetal energy demands. For some, this leads to gestational diabetes mellitus (GDM), a significant public health concern affecting ~14.0% of pregnancies worldwide. GDM is associated with adverse maternal and fetal health outcomes and notably increases the risk of maternal type 2 diabetes (T2DM) later in life. We investigated the contributions of maternal and fetal genetic variants to GDM and glycemic traits during pregnancy by performing the largest multi-ancestral GWAS meta-analyses of these traits to date.

Methods:
We analyzed i) GDM diagnosis (Nmaternal=38,375 cases, 776,075 controls; Nfetal=3,126 cases, 90,877 controls), ii) Fasting glucose (Nmaternal=55,371; Nfetal=15,855), iii) 1-hour glucose post-oral glucose tolerance test (OGTT) (Nmaternal=38,439; Nfetal=9,365), iv) 2-hour glucose post-OGTT (Nmaternal=46,401; Nfetal=15,046) and v) HbA1c (Nmaternal=9,724; Nfetal=7,035). Ethical approval was obtained for all studies. Downstream analyses included conditional analyses to partition maternal and fetal genetic effects and SCOUTJOY/shared variant analyses to distinguish GDM or T2DM-predominant effects at individual loci.

Results:
We identified 37 loci for GDM (29 novel) and 16 novel trait-variant associations for glycemic traits at genome-wide significance in the maternal meta-analyses. Conditional analyses suggested fetal GWAS signals were largely driven by maternal genotype correlations rather than fetal effects. Several genetic variants discovered were previously linked to glycemic traits outside pregnancy. LD score regression analyses supported substantial genetic overlap between GDM and T2DM (rG: 0.78), though 11 variants showed stronger associations with GDM than with T2DM, including variants at TENT5C, GCK, HKDC1, RMST, FOXA2, and NFATC2.

Conclusions:
Our findings provide new insights into the genetic architecture of GDM and glycemic traits during pregnancy, highlighting shared and distinct genetic influences that may inform future interventions.

Funding:
No funding received for this project.

Key-words: (up to 5):
Pregnancy, GWAS, Glycemic Traits, Gestational Diabetes.

Abstract #00004326 en

Maternal, neonatal, and biomarker factors linked to neonatal sepsis: observational study in a high-risk maternity hospital in the Brazilian Amazon.

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Campos Rosália de FátimaPenna de Carvalho (1), Vidigal Arícia de Azevedo (1), Azevedo Caio César Santana de (1), Gimenes Eleonôra Costa Monteiro (1), Roxo Pedro Lucas Brito Tromps (1), Carvalho Rafael Cardoso (2), Sousa Eduardo Martins (1)

(1) Graduate Program in Biosciences Applied to Health, CEUMA University—UNICEUMA, (2) Graduate Program in Health Sciences, Federal University of Maranhão—UFMA

Background/aims:

Background/aims: Neonatal sepsis is a major perinatal emergency associated with high rates of morbidity and mortality, especially in socially and obstetrically vulnerable settings. This study aimed to investigate the association between maternal and neonatal factors and the occurrence of sepsis, as well as to evaluate the diagnostic performance of laboratory biomarkers for this condition.

Methods:

Methods: This was a retrospective observational study involving 89 newborns hospitalized in 2024 at the High-Risk Maternity Hospital of Imperatriz (MARI), Brazil. Clinical and laboratory variables were analyzed using chi-square, Fisher's exact test, Mann-Whitney test, logistic regression, and ROC curves. The main outcome was the occurrence of neonatal sepsis. The project was approved by the Research Ethics Committee of University CEUMA (CAAE: 82312324.4.0000.5084; No. 7.046.286), in accordance with Brazilian Resolution CNS 466/12.

Results:

Results: Sepsis occurred in 61.8% of cases and was significantly associated with death (p=0.005). Maternal risk factors included fewer than six prenatal visits (aOR=7.25; p=0.007), prolonged rupture of membranes (aOR=9.60; p=0.005), and absence of intrapartum prophylaxis (aOR=6.32; p=0.007). Neonatal factors included vaginal delivery (aOR=4.16; p=0.011), prematurity, altered blood gas analysis (aOR=4.39; p=0.006), and gastric symptoms (aOR=6.03; p=0.008). Altered complete blood count (aOR=17.12; p<0.001) and elevated C-reactive protein (aOR=2.84; p=0.047) were significantly associated with sepsis. HMC and procalcitonin showed low diagnostic accuracy (AUC <0.60).

Conclusions:

Conclusions: Neonatal sepsis was strongly associated with early, modifiable perinatal exposures. Accessible clinical factors and basic biomarkers may support risk stratification and early intervention, aligned with the DOHaD framework.

Funding:

Funding: FAPEMA BEEP-02457/23 and CEUMA University.

Key-words: (up to 5):

Neonatal sepsis; Early life exposures; Biomarkers; Maternal risk; DOHaD.

Abstract #00004348 en

Maternal regulatory T cell deficiency in early pregnancy programs cardiometabolic dysfunction in male offspring.

Mechanisms Determining Transgenerational Effects of Health and Disease

Lovell Evangeline (1), Savin Stacey (1), Wooldridge Amy (2), Hosking Shanna (1), De Poi Rianna (1), Nicholas Lisa (1), Chapman Matthew (3), Surikow Sven (4), Parry Laura (2), Moldenhauer Lachlan (1), Robertson Sarah (1), Care Alison
(1)
(1) Robinson Research Institute and School of Biomedicine, University of Adelaide, (2) Robinson Research Institute and School of Biological Sciences, University of Adelaide, (3) Cardiology Unit, Lyell McEwin Hospital, Northern Adelaide Local Health Network, (4) Lyell McEwin Hospital and School of Medicine, University of Adelaide

Background/aims:
Offspring from preeclamptic pregnancies have an increased risk of cardiometabolic disease and immune dysfunction. Pregnancy complications like preeclampsia are associated with deficits in maternal regulatory T (Treg) cells, a subset of anti-inflammatory immune cells. We have shown that Treg cell deficiency in early pregnancy in mice causes uteroplacental dysfunction and fetal growth restriction, but the impact on cardiometabolic health in adult offspring is unknown. We evaluated whether maternal Treg cell deficiency in early pregnancy impairs offspring cardiometabolic parameters.

Methods:
Transgenic Foxp3DTR mice have FOXP3 promoter-driven expression of the human diphtheria toxin (DT) receptor, allowing selective depletion of FOXP3+ (Treg) cells upon DT administration. Foxp3DTR females mated to wild-type allogeneic BALB/c males were injected with DT (37.5ng/g) on gestational day (GD)3.5 and GD5.5 to deplete FOXP3+ cells; PBS-treated Foxp3DTR mice were controls. Treg cells or control T conventional (Tconv) cells were transferred into Treg cell-depleted mice on GD2.5 and GD4.5. Dams gave birth and offspring cardiometabolic health was evaluated by glucose tolerance test and echocardiography at 16-20 weeks of age.

Results:
Adult male (not female) offspring from DT-treated dams exhibited impaired glucose tolerance in adulthood (area under curve (AUC); P=0.02). Pre-treatment with Tregs but not Tconv cells in early pregnancy prevented this impairment, with AUC values similar to control offspring (AUC; P=0.99). Global longitudinal strain, an early indicator of left ventricular systolic dysfunction, was impaired in male (P=0.001) but not female offspring, and was mitigated by Treg cell supplementation (P<0.001).

Conclusions:
Maternal Treg cell deficiency in early pregnancy adversely affects fetal programming of cardiometabolic health in a sex-specific manner. This highlights the need to consider Treg cells as a target in inflammatory disorders of gestation to improve pregnancy outcomes and protect offspring cardiometabolic health.

Funding:
National Health and Medical Research Council (2002129), National Heart Foundation of Australia (101988) **Key-words: (up to 5):**

cardiometabolic, immune system, inflammation, fetal programming, regulatory T cells

Abstract #00004361 en

Maternal interesterified palm oil consumption impairs insulin sensitivity in skeletal muscle and liver of young and adult offspring

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Brasilio Villalta Paloma (1), Martins Fernandez Malentachi Luiza (1), Pedro Portela Lindoso João (1), da Nóbrega Baqueiro Mayara (1), Panzarin Carolina (1), Menta Penelope (1), Angélica de Paula Simino Laís (1), Martins Ignácio de Souza Letícia (1), Milanski Marciane (1), Alberto Torsoni Marcio (1), Souza Torsoni Adriana (1) (1) Unicamp

Background/aims:
The maternal nutritional environment during gestation and lactation plays a crucial role in the development of metabolic disorders in offspring. While interesterified fats are used as trans fat alternatives, they have been shown to disrupt insulin signaling. Nonetheless, the impact of maternal consumption of these fats and a subsequent exposure in adulthood on offspring metabolism is unclear.

Methods:
Female C57BL/6J mice were fed Natural Palm Oil (P) or Interesterified Palm Oil (I) for 4 weeks, then mated with standard chow-fed males. Offspring were weaned onto a P diet from day 21 until euthanasia (d30) or day 42 (d98). D98 offspring were divided into four groups during the following 8 weeks until euthanasia: PP, PI, IP, and II. Approved by the Animal Research Ethics Committee of the State University of Campinas (#5764-1/2021).

Results:
Body weight (BW) of I dams increased in weeks 2-3. Despite higher food intake in weeks 2–4, I dams exhibited increased energy expenditure in the last two weeks. During early lactation, P dams had higher BW, but by the end, both groups were similar. Offspring's BW did not differ, however, after weaning, I female offspring exhibited impaired glucose and insulin tolerance. At day 30, pAKT in the soleus was reduced in I offspring, while Akt gene expression was elevated in females but reduced in males. After a rechallenge, pAKT reduction was observed in PI and II (vs. PP/IP) with a similar pattern in hepatic pAKT in males. Oxidative stress analysis showed increased SOD activity and MDA concentration in the IP and II liver (vs. PP/PI).

Conclusions:
Interesterified palm oil may impact only dams' murinometric parameters. However, glucose homeostasis and insulin signaling in skeletal muscle appear to be disrupted in early life and further molecular changes in the liver with a rechallenge.

Funding:
CAPES (#001) and FAPESP (#23/02026-9)

Key-words: (up to 5):
DOHaD; Maternal Diet; Interesterified Fat; Insulin Resistance; Oxidative Stress

Abstract #00004362 en

A psychologist in perinatal care: positive effects on maternal postpartum mental wellbeing?

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Brinkman Evie (1), Mulders Peter (2), de Weerth Carolina (1)
(1) Radboudumc, (2) radboudumc

Background/aims:
More than 1 in 5 pregnant women in community populations show clinically meaningful mental health (MMH) problems. Unfortunately, these problems frequently go unnoticed and untreated, possibly developing into more serious MMH problems with far-reaching consequences for both mother and child. Early detection and treatment of these problems is therefore needed. Here we investigate the effects of having a psychologist in standard perinatal care on maternal postnatal mental health

Methods:
Using a two-period cross-over design, two groups of women (N=680) recruited in early pregnancy will be compared: 1) an intervention group routinely screened for MMH problems and offered psychologist counselling, and 2) a control group receiving care as usual. All participants gave written consent (NL84354.091.23/ 50-54300-98-604). Analysis of Covariance (ANCOVA) will be used to investigate the effect of the group (psychologist or control) on 1. self-reported general mental wellbeing, 2. parental mental wellbeing, and 3. birth trauma. The effect of receiving psychologist care on maternal mental health trajectories from pregnancy to the postpartum period will be investigated using growth mixture modelling. Moreover, using linear regression we will investigate whether the intervention moderates the link between MMH problems and mental healthcare consumption.

Results:
It is hypothesized that women who were offered psychological counselling will have higher self-reported general mental wellbeing and parental mental wellbeing, and lower birth trauma compared to women receiving care as usual.

Conclusions:
Implementing a perinatal psychologist in current perinatal care is expected to have a positive effect on mental health, decreasing MMH problems and preventing more severe psychiatric disorders.

Funding:
ZonMw (project 05430052110008)

Key-words: (up to 5):

Abstract #00004363 en

Impact of maternal obesity on offspring hypothalamic development and feeding behaviour: role of fetal hyperinsulinemia

Mechanisms Determining Transgenerational Effects of Health and Disease

Dearden Laura (1), Wong Wai Ping (1), Chong Rosanne (1)
(1) University of Cambridge

Background/aims:
Animal models show that obesity in offspring exposed to maternal obesity is driven by hyperphagia. The hypothalamus is the key area of the brain involved in regulation of feeding behaviour, and its development is dependent on metabolic signals. Therefore, in utero exposure to the altered metabolic milieu of maternal obesity and GDM could permanently disrupt hypothalamic development. Maternal obesity during pregnancy is associated with maternal and fetal hyperinsulinema, which may drive disrupted fetal development. We aim to test whether elevated fetal insulin disrupts hypothalamic development in offspring from obese pregnancies, leading to dysregulated food intake.

Methods:
We used a mouse model of maternal diet- induced obesity in pregnancy. The effect of insulin on hypothalamic neural progenitor cell (NPC) proliferation was evaluated via neurosphere assays and immunofluorescence. Hypothalamic insulin signalling was assessed by western blot. Feeding behaviour in adult offspring from control and obese pregnancies were assessed using fast-refeed and ad-lib feeding studies. These studies have been approved by the Animal Welfare and Ethics Review Board.

Results:
Fetal hypothalamic NPCs from obese pregnancies have reduced proliferative potential and are resistant to the proliferative effects of insulin in vitro. Proliferation of hypothalamic NPCs is negatively corelated with dam insulin levels. We found in vivo evidence of insulin resistance in the fetal hypothalamus of offspring exposed to maternal obesity. These molecular changes are associated with disrupted feeding behaviour in offspring of obese dams, including increased rebound feeding after fasting, increased ad-lib intake of a HFD (at 8 weeks old) and increased ad-lib intake of a chow diet (at 12 months old). Exercise in obese dams reduces fetal hyperinsulinemia and rescues offspring hyperphagia.

Conclusions:
Exposure to maternal obesity in utero is associated with fetal hypothalamic insulin resistance and long-term changes to feeding behaviour.

Funding:
Rosetrees Trust, Royal Society and Wellcome

Key-words: (up to 5):
hypothalamus, obesity, food intake, insulin

Abstract #00004384 en

Assisted reproductive technology and offspring internalising/externalising symptoms: An individual participant data meta-analysis

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Cui Naixue (1), Soares Ana Goncalves (2), Bond Tom (2), Cadman Tim (3), Vrijkotte Tanja G (4), Lawlor Deborah A (2), Elhakeem Ahmed (2)
(1) Shandong University, (2) University of Bristol, (3) University Medical Centre Groningen, (4) University of Amsterdam

Background/aims:
There are concerns that assisted reproductive technology (ART) may have adverse effects on offspring mental health. However most previous studies rely on small and selected samples and short follow-up duration. This study aimed to examine ART conception's effect on offspring internalising and externalising symptoms across childhood and adolescence.

Methods:
Unselected general population birth cohort studies were recruited from the A.R.T-HEALTH-PARTNERHSIP. To be included, studies had to have data on whether offspring was conceived by ART or naturally (NC), offspring internalising/externalising symptoms at any age, and key confounders (maternal age at conception, socioeconomic position, and parity). Continuous internalizing/externalising symptoms scores were mostly derived from parent-reported Strengths and Difficulties Questionnaire. Analyses were done separately in each cohort using standard statistical code, with results combined in meta-analysis by age groups.

Results:
More than 20 studies in Europe, Asia, and Canada were included. Preliminary meta-analysis in three studies in the UK and Netherlands (N-TOTAL=19,098; N-ART=248) shows that ART conception (vs. NC) associated with higher parent-reported offspring internalising symptoms at age 3–6y (pooled adjusted mean difference: 0.18SD, 0.06 to 0.30, I2=0), 7–10y (0.15SD, 0.007 to 0.30, I2=0), 11-14y (0.16SD, 0.006 to 0.31, I2=0), and 15-18y (0.18SD, -0.10 to 0.46, I2=58.4%). Conversely, ART was not associated with externalising (pooled difference from -0.03SD to 0.04SD).

Conclusions:
Preliminary findings suggest that ART conception associates with higher parent-reported offspring internalising, but not externalizing, symptoms in childhood and adolescence. Cohort analyses in the remaining studies are currently ongoing. Planned secondary and sensitivity analyses will examine the role of parental infertility, differences in associations by type of ART, sex, and informant. Differences in association by age and cohorts will also be examined.

Funding:
European Research Council.

Key-words: (up to 5):
ART; mental health; emotion; behavior; birth cohort

Abstract #00004398 en

Milk Matters: Comparing Body Composition in Preterm Neonates Fed Pasteurized Human Donor Milk vs. Mother's Own Milk

Role of Infant and Young Child Feeding Practices on Long-Term Health

Bhaskaracharya Archana (1), Esvaran Meera (1), Downe Lyn (1), Deshpande Girish (1) (1) Nepean Hospital, NSW Health, Penrith, Australia

Background/aims:
The pasteurized donor human milk (PDHM) is used routinely when Mother's own milk (MOM) is insufficient. Clinical benefits of PDHM include reduced NEC, infections and feed intolerance, however impaired growth rates due to low protein and energy content have also been reported. Factors such as pooling milk multiple donors influence may help, however in Australia, PDHM supplied by Australian Red Cross milk bank service is not pooled.
Aim-evaluate the impact of PDHM feeding on body composition of preterm neonates as compared to MOM at Nepean NICU, Sydney Australia.

Methods:
This prospective observational study approved by NMBLHD ethics committee (HREC/15/NEPEAN/91). Preterm neonates born <32 weeks or birth weight <1500g between March-2016 and November-2023 and received either PDHM or MOM who underwent air-displacement plethysmography (PeaPod®) body composition analysis at discharge were analysed. The impact of PDHM enteral nutrition on body composition evaluated by comparing with MOM group. R-package was used. General linear model employed to evaluate statistically significant differences of fat mass (FM), fat free mass (FFM), and between groups after adjusting for gestational age, birth weight, gender, weight gain from birth to discharge.

Results:
Total 99 neonates were included in the analysis, 53 (25 male; 28 female) neonates in MOM (received >80% MOM) and 46 (29 male; 17 female) neonates in PDHM group. Gestational age and birth weight were comparable in both groups. Significantly higher % FM, FM and reduced FFM were observed in the PDHM group. Hospital stay was longer for PDHM neonates (63 days; 43- 93 days) as compared to MOM group neonates (63 days; 41- 73 days).

Conclusions:
The body composition results show that there was significant reduction in fat free mass and increased fat mass in preterm neonates receiving PDHM. Our findings suggest that fortification strategies to offset the lower and variable protein and energy content of PDHM may lead to improved outcomes.

Funding:

Key-words: (up to 5):
Preterm neonate, human milk, body composition

Abstract #00004405 en

Exposure of a single dose of dexamethasone on postnatal day 3 causes behavioural, neuropathological and metabolic changes in adolescent rats

Impact of Early Life Exposures and Environmental Pollutants

Pajak Rachael (1), Almushri Khairiah (1), Fletcher Jennifer (1), Glazier Jocelyn (1), Myers Jenny (1), Hager Reinmar (1), Harte Michael (1)
(1) University of Manchester

Background/aims:
Dexamethasone is given to mothers at risk of preterm birth to improve infant survival and lung development. However, emerging evidence suggests it may impair neurodevelopment, behaviour and metabolism later in life. We investigated the effect of early postnatal administration of dexamethasone on behavioural, molecular and metabolic outcomes in male and female adolescent rats.

Methods:
Wistar rats received a subcutaneous injection of dexamethasone (0.2, 0.5, and 1 mg/kg) or saline on postnatal day (PN) 3, corresponding to preterm infant brain development. Rats (n=4/sex/dose) were sacrificed 60-90 minutes post-injection to measure brain dexamethasone levels via Liquid Chromatography-Mass Spectroscopy (LC-MS). A separate cohort (n=10/sex/dose) underwent behavioural testing in adolescence (PN35-40), including novel object recognition (NOR) for cognition, social interaction (SI), and light-dark box (LDB) and open field test (OFT) for anxiety-like behaviours. GABAergic and synaptic markers were analysed in the dorsal hippocampus.

Results:
LC-MS confirmed dose-dependent brain penetrance. When compared to vehicle treated animals, administration of dexamethasone on PN3 led to an increase in time spent in the light zone in the LDB (0.2, 0.5 & 1 mg/kg all $p<0.001$), an increase in locomotor activity (0.2, 0.5 & 1 mg/kg,$p<0.01$) and an increase in social interaction (0.2 & 1 mg/kg,$p<0.018$ and $p<0.024$). We observed no significant changes in NOR or OFT. Post-mortem brain analysis revealed significant deficits in GAD67 ($p<0.05$) and PSD95 ($p<0.05$), with no change in parvalbumin or SNAP25 ($p>0.05$). Rats also developed polydipsia and polyuria traits.

Conclusions:
Administration of dexamethasone during a critical development window induced a hyperactive, disinhibited behavioural phenotype in adolescent rats. These behavioural changes were accompanied by neuropathological and metabolic alterations. Ongoing research will determine whether these effects persist into adulthood alongside further investigations to characterise the diabetic-like phenotype observed.

Funding:
Kennedy Trust

Key-words: (up to 5):
glucocorticoids; behaviour; neurodevelopment; stress

Abstract #00004410 en

FETAL PROGRAMMING BY ANDROGEN EXCESS IMPAIRS OVARIAN FUNCTION IN ADULT LIFE

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Silva Aimé (1), Higa Romina (1), Motta Alicia (1)
(1) CEFyBO - CONICET

Background/aims:
Prenatal androgen excess is a key factor in the development of Polycystic Ovary Syndrome (PCOS), a disorder characterized by endocrine and metabolic alterations that lead to uterine and ovarian dysfunctions, resulting in infertility and early pregnancy loss. We investigated the impact of fetal programming by prenatal androgens on adult ovarian function, focusing on transcription factors (PPARα, PPARγ, and EGR1), hormonal and gonadotropin receptors (AMHr, FSHr, LHr, androgen AR, estrogen ESr1, ESr2, and progesterone PRα, and PRβ) and follicular count.

Methods:
Pregnant Sprague-Dawley rats (F0) were injected with testosterone (1 mg/100 µL oil) or vehicle to generate prenatally hyperandrogenized (PH, n=10) and control (n=10) offspring (F1), respectively. At 90 days of age, female rats were euthanized during estrus, and ovarian tissue was isolated. All procedures were approved by CICUAL (RES35412022).

Results:
Protein expression of PPARα remained unchanged, while PPARγ, a master regulator of FSHr, was upregulated in PH ovaries (Fold Change (FC)=2.0; $p<0.05$). The mRNA levels of EGR1, modulator of steroidogenesis, ovulation, and gonadotropin receptor expression were downregulated (FC=0.5; $p<0.05$ vs controls). FSHr and LHr mRNA levels were significantly elevated in PH animals (FC=2.2, $p<0.01$; and FC=3.1, $p<0.03$, respectively), as were ESr1 (FC=1.9, $p<0.05$) and PRβ (FC=2.7, $p<0.05$) compared to controls. Furthermore, follicular analysis revealed a significant increase in preantral follicles ($p<0.02$) and cysts ($p<0.05$), and a decrease in antral ($p<0.01$), Graafian follicles ($p<0.03$), and corpora lutea ($p<0.02$) in the PH group compared to controls.

Conclusions:
Prenatal hyperandrogenism induces regulatory changes that increase gonadotropin sensitivity and disrupt ovulation. Altered follicular dynamics, along with changes in hormonal receptors and transcription factors expression, suggest that androgen excess during fetal life programs long-term ovarian dysfunction, potentially underlying the subfertility observed in PCOS.

Funding:
Proyectos de Investigación Plurianuales (PIP) 1872, 2021 from CONICET.

Key-words: (up to 5):
Polycystic Ovary Syndrome, Fetal Programming, Ovarian Functions, Transcription Factors, Hormonal Receptors.

Abstract #00004420 en

Elevated dietary fat exposure in early development and the prolonged impact on brain activity: Response to acute dietary and therapeutic interventions in adulthood.

Impact of Early Life Exposures and Environmental Pollutants

Lippert Rachel (1), Yagoub Selma (2), Chesters Robert (2), Ritter Katrin (2)
(1) German Institute Of Human Nutrition , (2) German Institute of Human Nutrition

Background/aims:
The brain primarily regulates energy balance through the central melanocortin system. We aimed to understand the role of the paraventricular nucleus of the thalamus (PVT), a brain region involved in integrating energy state with behavior, and how early nutritional influences impact this system. The melanocortin-3-receptor (MC3R), a key player, is highly expressed within the PVT. We investigated the effects of early overnutrition and how it impacts MC3R neuronal development and activity.

Methods:
We used a model where offspring are exposed to a high-fat diet (HFD) from the mother during lactation. We compared these offspring to those whose mothers received a matched control diet. We examined the brain's structure using immunohistochemical techniques to visualize neuropeptides, axonal projections and neuronal activation. To further assess activity, we used fiber photometry to measure MC3R neuronal activity in a subset of offspring. Adult offspring were then challenged with either a high-fat diet (48 hrs), fasting-refeeding or pharmacological intervention with Setmelanotide (an alpha-melanocyte stimulating hormone (α-MSH) mimetic), allowing us to observe and measure any resulting brain changes.

Results:
We identified a role of early maternal overnutrition in impacting the maintenance of projections to the PVT and assessed changes in neuronal response. We observed changes in the structure and activity of MC3R neurons linked to their early developmental nutritional exposure.

Conclusions:
This research highlights the crucial role of early nutrition in shaping the brain's response to metabolic challenges. Further study of MC3R neurons in the PVT could improve our understanding of offspring feeding behaviors impacted by maternal diet. More research is needed to explore these findings in humans and how early nutrition can impact adult brain responses.

Funding:
Leibniz Competition Best Minds Grant 'BAByMIND' J99/2020, DFG EXC-2049 – 390688087 (NeuroCure), DZD 82DZD03D2Y

Key-words: (up to 5):
feeding, brain, maternal nutrition, PVT, melanocortin 3 receptor

Abstract #00004426 en

Investigating the effect of neonatal dexamethasone exposure on behavioural and neuropathological outcomes in male and female offspring

Impact of Early Life Exposures and Environmental Pollutants

Almushri Khairiah (1), Fletcher Jennifer (1), Glazier Jocelyn (1), Hager Reinmar (1), Grayson Ben (1), Harte Michael (1) (1) University of Manchester

Background/aims:
Dexamethasone is commonly used between 24-34 weeks of gestation to reduce preterm birth risks. However, use after 36 weeks may adversely affect neurodevelopment, leading to long-term cognitive and neuropathological impairments. This study investigates the effect of administration of dexamethasone at postnatal day (PND) 7 (corresponding to late pregnancy in humans in relation to brain development) on behavioural and neuropathological outcomes in adolescent and adult offspring using a rodent model

Methods:
Male and female Wistar rats were administered 0.9% saline or dexamethasone (Dexa) (0.2, 0.5 or 1 mg/kg,SC) or left untreated on PND 7. After 90 minutes, offspring (n=45) were culled, and brains were collected to measure dexamethasone concentration using Liquid chromatography-mass spectrometry (LC–MS). Behavioural assays, including novel object recognition (NOR) and light/dark box (LDB) and social interaction (SI) were conducted on adolescent (n=100) and adult (n=100) offspring. Synaptic and neuronal markers were assessed in the dorsal hippocampus. Data were analysed by one-or two-way ANOVA followed by post-hoc analysis

Results:
Dexamethasone concentration was significantly increased in the PND7 rats' brains ($p<0.05$-0.001). 0.2 mg/kg Dexa caused cognitive deficits in NOR performance in adolescent and adult female offspring, while other groups demonstrated typical novel object preferences ($P<0.01$-<0.001). In LDB, Dexamethasone reduced the dark zone preference ($P<0.05$-<0.001) in adolescent and adults, and increased locomotor activity ($p<0.05$-0.01) in adolescents. In SI, male offspring treated with Dexa showed a reduction in sniffing ($p<0.001$). No changes were observed in GABAergic markers, but synaptic markers were reduced in the dorsal hippocampus in adolescents and adults ($P<0.05$-<0.01)

Conclusions:
Administration of dexamethasone on PND7 causes behavioural and neuropathological alterations that persist into adolescence and adulthood, indicating a reduced anxiolytic/disinhibited phenotype alongside a reduction in synaptic markers in the brain

Funding:

The Custodian of the Two Holy Mosques' External Scholarship Program, Saudi Arabia Cultural Bureau

Key-words: (up to 5):
Dexamethasone Behaviours Neuropathology PND7

Abstract #00004428 en

Inhibition of Hypoxia-Inducible Factor-1 (HIF-1) impairs mouse luteal function without effect on fertility

Plant and Animal Health and Its Impact on Reproductive Age Individuals and Their Offspring

Marinoni Rocío Celeste (1), España De Marco María José (1), Velazquez Candela (1), Bordaquievich Mayra (1), Prost Katherine (2), Tesone Marta (1), Abramovich Dalhia (1)
(1) IBYME - CONICET, (2) Hospital Interzonal General Agudos Pedro Fiorito

Background/aims:
Ovarian angiogenesis plays a crucial role in the development of both follicles and corpora lutea. Hypoxia-inducible factor-1 (HIF-1) is the primary regulator of angiogenesis, with the ability to detect reduced oxygen levels.
The objective of our study was to elucidate the role of HIF-1 in the ovary during luteinization and in female fertility.

Methods:
Prepubertal female F1 mice (BALB/c x C57) received 5 IU of eCG i.p. followed by 5 IU of hCG i.p. 48h later. A group of animals received i.p. 5 mg/kg of the HIF-1 inhibitor Acriflavine (ACF) the day of hCG injection (Low Dose ACF) and another group received i.p 10 mg/kg of ACF both the day of hCG injection and the following one (High Dose ACF). 48h after hCG, mice were sacrificed and the ovaries and serum recovered. A group of 2-month-old female F1 mice was treated with 10 mg/kg ACF i.p. (High Dose ACF). Subsequently, the animals were mated. Upon confirmation of pregnancy, the females were administered 10 mg/kg ACF i.p again. Control group received PBS. The study assessed time to pregnancy, duration of gestation, litter size and offspring weight.
Animal experiments were approved by The Animal Experimentation Committee of IByME–CONICET (Protocol #29/2021).

Results:
Ovarian VEGF was decreased in both ACF groups and HIF-1α was decreased only in High Dose ACF. Endothelial and periendothelial cell areas were diminished within the corpora lutea of both ACF groups. There was an increase in aberrant structures in the High Dose ACF group. Serum progesterone decreased in the High Dose ACF group, along with ovarian StAR levels. The percentage of corpora lutea suffering luteolysis increased in High Dose ACF animals.
Females treated with ACF during early corpus luteum formation showed no alterations when mated with fertile males.

Conclusions:
HIF-1 inhibition affects luteal function, with no effect on fertility.

Funding:
PICT 2020-2111; PIP 2022-927

Key-words: (up to 5):
CORPUS LUTEUM, HYPOXIA-INDUCIBLE FACTOR-1, ANGIOGENESIS, ACRIFLAVINE

Abstract #00004444 en

DOHaD knowledge survey among healthcare professionals and advanced students

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Lin Chuan Chuan (1), López Laura (1), Gorelik Berta (1), Roussos Adriana (1), Arias Lilia (1), Barretto Luciana (1),
Pérez Mariana (1), Tonietti Miriam (1)
(1) Sociedad Argentina de Nutrición

Background/aims:
Research on the Developmental Origin of Health and Disease (DOHaD) has demonstrated that the health and development of the next generation can be influenced by environmental factors from preconception to early childhood. Adverse environmental influences during these early periods have been shown to increase the risk to develop noncommunicable diseases (NCDs) such as obesity, cardiovascular disease, and type 2 diabetes later in life.
Furthermore, there is increasing evidence that NCDs can be prevented by early life intervention.
Objective: To Examine the knowledge, attitudes, and practices (KAP) of medical students, residents and professionals in Obstetrics and Gynecology, Pediatrics and Nutrition from Argentina about the DOHaD concept.

Methods:
Participants were invited to answer a multi-section questionnaire, including: Knowledge (eight questions on the definition and clinical implications of DOHaD concept); Attitude (six questions on beliefs and confidence levels in counseling patients about healthier lifestyles to improve the health of mothers and future generation of offsprings); Practice (six questions on current practices of counseling patients about the impact of current parental and child metabolic health on future health). Demographics including age, sex, and medical specialty were collected.

Results:
Of 174 respondents, 55,7% were unsure about their understanding or didn´t know the DOHaD concept. One-third rated their knowledge of DOHaD as poor, and two-thirds believed that the information their colleagues or other healthcare professionals had about DOHaD was also poor. 90% were aware that exposures in the early intrauterine environment are associated with long-term risk of noncommunicable diseases in the first generation, but 40% were unsure or disagreed that it affects subsequent generations.
Approximately 90% of respondents were interested in receiving training on DOHaD-related topics.

Conclusions:
It is essential to improve training in the DOHaD concept for healthcare professionals (especially pediatricians, obstetricians and gynecologists) and to develop an interdisciplinary implementation framework to apply the DOHaD concept in clinical practice.

Funding:
Key-words: (up to 5):
DOHaD knowledge attitudes practices

Abstract #00004446 en

Probability of becoming a parent after being born preterm and small for gestational age - a registry based study in a Nordic population

Big Data and Cohorts in DOHaD Research.

Metsälä Johanna (1), Opdahl Signe (2), Alenius Suvi (1), Pulakka Anna (3), Yin Weiyao (4), Gissler Mika (5), Risnes Kari (6), Sandin Sven (4), Kajantie Eero (1)

(1) Clinical Medicine Research Unit, University of Oulu, Oulu, Finland, (2) Department of Public Health and Nursing, NTNU, Trondheim, Norway, (3) Research Unit of Population Health, University of Oulu, Oulu, Finland, (4) Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden, (5) Department of Data and Analytics, Finnish Institute for Health and Welfare, Helsinki, Finland, (6) Department of Clinical and Molecular Medicine, NTNU, Trondheim, Norway

Background/aims:

Adults born preterm or with low birthweight are less likely to have children, but the specific roles of preterm birth and fetal growth restriction are unclear.

Methods:

The study included 3,296,584 women and 3,487,347 men born in Finland (1987-2007), Norway (1967-2008), and Sweden (1974-2008), followed from age 13 years until the birth of their first liveborn child or end of follow-up (2020/2021). Exposure categories were gestational age <32, 32-33, 34-36, and ≥37 weeks (term), with and without small for gestational age (SGA). Adjusted, sex-specific hazard ratios (HRs) were pooled. Follow-up was split at age 30 years. Informed consent was not required.

Results:

Throughout follow-up and irrespective of SGA status, women born preterm were less likely to have children than term-born women without SGA. For example, women born <32 weeks with SGA had HR 0.73 (95% confidence interval 0.70-0.76) before and 0.64 (0.55-0.74) after 30 years. Term-born women with
SGA were more likely to have children before 30 years (1.03, 1.03-1.04) but less likely after 30 years (0.89, 0.88-0.90). Men born preterm were less likely to have children at all ages, and being born SGA further reduced this likelihood. For example, from age 30 years, men born <32 weeks without SGA had HR
0.64 (0.61-0.68), whereas men born <32 weeks with SGA had HR 0.48 (0.42-0.56).

Conclusions:

Women born at the lowest gestational ages are least likely to have children, with SGA not further affecting this association. Term-born women with SGA are more likely to have children before age 30 but less likely after age 30. Among men, SGA further decreases the likelihood of having children in addition to lower gestational age.

Funding:

Research Council of Finland (354936), Signe and Ane Gyllenberg Foundation, Paulo Foundation, Jalmari and Rauha Ahokas Foundation

Key-words: (up to 5):

Preterm birth, SGA, reproduction, fertility

Abstract #00004456 en

Association of Low Birth Weight, Childhood Adversity, and Natural Disaster with Delay Discounting among Children

Impact of Early Life Exposures and Environmental Pollutants

Terada Shuhei (1), Maeda Yuto (1), Surkan Pamela J. (2), Fujiwara Takeo (1)
(1) Institute of Science Tokyo, (2) Johns Hopkins University,

Background/aims:
The DOHaD hypothesis suggests that low-birthweight (LBW) infants are programmed to seek additional resources as a compensatory mechanism for early deprivation in utero. However, no studies have explored this concept in relation to delay discounting, which refers to the tendency to prefer smaller, immediate rewards over larger, delayed ones. Furthermore, postnatal factors such as adverse childhood experiences (ACEs) and exposure to natural disasters may also influence delay discounting. This study aimed to examine the association of LBW, ACEs, and natural disaster exposure with delay discounting among children.

Methods:
This prospective cohort study recruited 167 children from areas affected by the 2011 Great East Japan Earthquake (GEJE). Birthweight and ACEs before and after the GEJE were assessed using caregiver-reported questionnaires collected at baseline in 2012. Traumatic experiences during the GEJE were assessed through semi-structured interviews by child psychiatrists or psychologists. In 2014, delay discounting was evaluated using a token-based experiment in which children (mean age: 8.3 years) were initially given 5 tokens to allocate for either immediate rewards (one candy per token “now”) or delayed rewards (two candies per token “one month later”). The dependent variable was the number of tokens allocated for the "now" option. Multivariable Poisson regression models were used to estimate the incidence rate ratios (IRRs) for each exposure.

Results:
Children with LBW were 0.68 times less likely to allocate tokens for immediate rewards (95% CI: 0.46-1.00). Similarly, children with three or more ACEs before the GEJE were less likely to choose immediate rewards (IRR: 0.58, 95% CI: 0.37-0.91). No associations were found between ACEs after GEJE or traumatic experiences during the GEJE and token allocation.

Conclusions:
Children with LBW and multiple ACEs before the GEJE showed lower delay discounting (greater patience), suggesting adaptive strategies to prioritize long-term rewards regardless of timeline.

Funding:
This work was supported by a grant from the Ministry of Health, Labour and Welfare (H24-jisedai-shitei-007, H25-seiiku-shitei-00x, H28-sukoyaka-shitei-003, H28-kodomokosodate); Japan Society for the Promotion of Science (19H04879); and Meiji Yasuda Mental Health Foundation (H28).

Key-words: (up to 5):
Adverse childhood experiences, Delay discounting, Great East Japan Earthquake, Low birthweight

Abstract #00004457 en

Awareness of folic acid intake during pregnancy and DOHaD among Japanese pharmacy students

Public Health Policies Across the Life Cycle.

Iwazawa Haruna (1), Joda Mayumi (1), Mizuoka Daisaku (1), Yamaguchi Kazunori (2), Motoki Takahiro (1), Tanaka hiroaki (1), Kosaka Shinji (1)
(1) Department of Pharmacy, Kagawa university hospital, (2) Safety Management office, Kagawa university hospital

Background/aims:
Folic acid, a vitamin particularly important for the normal development of the fetus, is closely linked to the concept of the Developmental Origins of Health and Disease (DOHaD). However, in Japan, the low rate of folic acid intake remains a concern. One potential reason for the low intake of folic acid supplements among pregnant women in Japan is the lack of awareness among healthcare professionals, including pharmacists. This study aims to clarify the extent to which pharmacy students,who are expected to provide guidance on folic acid intake and supplement use in the future, understand the importance of perinatal folic acid intake and the concept of DOHaD.

Methods:
The study participants were 25 pharmacy students receiving clinical training at Kagawa University Hospital. The survey was conducted using a self-administered questionnaire. This study was approved by the Ethics Committee of Kagawa University Faculty of Medicine.

Results:
Sixteen students (64%) were aware of the importance of folic acid intake during pregnancy. The most common source of information was “university lectures,” followed by “pharmacists” and “the Internet.” However, only two students (8%) knew the appropriate amount of folic acid intake. Additionally, only one student had heard of the term DOHaD.

Conclusions:
Although nutritional science is incorporated into the pharmacy curriculum in Japan, the information provided to pharmacy students regarding the importance of folic acid intake during the perinatal period may be insufficient. It is necessary to further promote provision of information on supplements and nutrition in pharmacy education. Moreover, pharmacists are expected to play a more effective role in supporting pregnant women and contribute to appropriate folic acid intake during the perinatal period.

Funding:

Key-words: (up to 5):
Folic acid

Abstract #00004474 en

Breast milk modulates insulin sensitivity in offspring born from hyperglycemic dams in a rodent model

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Bobin Paul (1), Grit Isabelle (1), Massias Corentin (1), de Coppet Pierre (1), Castellano Blandine (1), David-Sochard Agnès (1), Cloteau Chloé (2), Croyal Mikaël (2) (3), Le Dréan Gwenola (1), Alexandre-Gouabau Marie-Cécile (1)
(1) Nantes Université, INRAE, UMR 1280, PhAN, CRNH-OUEST, IMAD, F-44000 Nantes, France., (2) Nantes Université, CNRS, INSERM, L'institut du Thorax, Nantes, France , (3) Nantes Université, CHU Nantes, Inserm, CNRS, SFR Santé

Background/aims:
Gestational Diabetes Mellitus (GDM) increases type 2 diabetes risk in the offspring later in life. In a context of GDM, whether breast milk bioactive compounds support offspring pancreatic β-cell proliferation and maturation, promoting healthy glucose metabolism and reducing the risk of adulthood metabolic disorders, remains unclear.

Methods:
GDM-impaired glucose tolerance (IGT) was induced in a cross-fostering rat model dams fed High-Fat, High-Sucrose diet during gestation (4HFHS) or gestation and lactation (7HFHS) compared to those under Control diet (CTL). Milk metabolome and lipidome were analysed at Postnatal Day (PND)1 and PND14. Breast milk impact on glucose homeostasis were investigated in GDM-offspring nursed by foster dams with IGT-corrected (4HFHS) or not (7HFHS) postpartum and compared to those nursed by CTL. Pancreatic islet gene expression was quantified by RT-qPCR in offspring at birth, PND14 and PND220. Oral Glucose Tolerance Tests (OGTT) and euglycemic-hyperinsulinemic clamps were performed at PND220. Animal experiments have been approved by an ethics-committee.

Results:
Colostrum from 4HFHS and 7HFHS had higher levels of insulino-trophic compounds (valine, leucine and oleic acid) and long-chain sphingolipids compared to CTL dams. At PND14, these compositional differences were maintained in 7HFHS compared to 4HFHS milk. At birth, GDM-pups presented islet hypertrophy and hyperplasia associated with a lower β-/α-cell ratio. At PND14, GDM-pups nursed by 7HFHS (HH) versus 4HFHS (DG) dams presented higher expression of NeuroD1 (endocrine differentiation), GLUT2 and insulin genes beside enhanced non-fasting glycemia and insulinemia. At PND220, male GDM-offspring nursed by CTL dams (HC) showed hyperglycemia during OGTT associated with higher 2 hours-insulinemia, while insulin and amylin gene expression were decreased. Systemic insulin-sensitivity in response to hypercaloric challenge tended to be lower in female HC.

Conclusions:
Hyperglycemia during pregnancy is associated with adaptation of maternal milk composition, that may have offspring repercussions on β-cell maturation and adult metabolic trajectories depending on maternal glucose tolerance during lactation.

Funding:

ANR-22-CE17-0039-GDM-MILK; INRAE AlimH; Région Pays de la Loire; Société Française de Néonatologie The authors certify that the conditions for submission have been satisfied and that all animal welfare and ethical considerations have been met.

The experimental protocol was carried out in accordance with current institutional guidelines on animal experimentation in the EU (directive 2010/63/EU) and in France (French Veterinary Department—A44276) and the 3Rs (Replacement, Reduction, Refinement) principle. All animal procedures were approved by the Animal Ethics Committee of Pays de La Loire and the approval from the French Ministry of Superior Education and Research (APAFIS #35043-2022011317589759v6)"

Key-words: (up to 5):
Gestational Diabetes Mellitus, Breast milk, Pancreas, β-cell maturation

Abstract #00004475 en

A Data-Driven approach for optimizing gestational weight gain (GWG) by age and BMI

Big Data and Cohorts in DOHaD Research.

Asres H (1), Ram U (2), Thirunavukkarasu M (3), S Nishanth (3), Sukumar N (4), Saravanan P (4), Ghebremichael-Weldeselassie Yonas (5)
(1) School of Mathematics and Statistics, The Open University, UK , (2) Seethapathy Clinic and Hospital, Chennai, India ; Fetal Care research Foundation, Chennai, India , (3) Seethapathy Clinic and Hospital, Chennai, India , (4) Warwick Academic Health, Warwick Medical School, University of Warwick, UK , (5) School of Mathematics and Statistics, The Open University, Milton Keynes, UK ;

Background/aims:
To develop a data-driven method for selecting optimal GWG intervals stratified by maternal age and Asia-Pacific BMI categories that improves healthy pregnancy (HP) outcomes.

Methods:
The IOM guidelines were based on systematic literature review and modeling to balance risks across pre-pregnancy BMI categories. They do not stratify by maternal age or optimize HP probabilities. We applied a data-driven method for stratified GWG recommendations by age and SA-specific BMI. HP was defined as a live, appropriate-for-gestational-age (AGA) birthweight without prematurity or emergency cesarean, outcomes identified by the IOM. Assuming a quadratic relationship, HP probability was estimated at each GWG value using logistic regression with 10-fold cross-validation repeated five times, then weighted by GWG density. Probabilities were divided into high- and low-probability groups using Jenks natural breaks. For each interval, created using a 1–10kg sliding window (0.5kg increments) across GWG, the harmonic mean (HM) of the proportions of HP from the high-probability group within the interval and the non-HP from the low-probability group outside the interval was calculated. GWG was categorized as within or outside each interval. Logistic regression assessed associations with HP, adjusting for parity, GDM, and preeclampsia. The interval with the highest HM score and significant improvement in HP was selected. The method was validated using a cohort of 13,870 singleton pregnancies from India.

Results:
The new recommended GWG (kg) ranges were: 18–25years: (9.5–12.5, 9.0–15.5, 6.6–12.6), 26–30years: (8.1–13.1, 8.7–11.7, 5.4–11.4), and >30years (5.5–11.5, 4.9–5.9, –4.8 to –2.8) for normal, overweight, and obese categories, respectively. These intervals were lower than IOM guidelines (normal:11.5–16, overweight:7.0-11.5 and obese:5.0-9.0kg). The HP rates were generally higher in the new guidelines.

Conclusions:
This novel data-driven, age- and BMI-stratified method provides personalized GWG guidelines associated with higher HP outcomes for Indian women.

Funding:
School of Mathematics and Statistics, The Open University, and Open Societal Challenge Fund, The Open University, Milton Keynes, UK.

Key-words: (up to 5):
Gestational weight gain, healthy pregnancy, interval selection, harmonic mean, IOM guidelines

Abstract #00004479 en

Placental 11β-HSDs levels in gestational diabetes and metabolic health in early childhood

Impact of Early Life Exposures and Environmental Pollutants

Yang Meng-nan (1)
(1) Xinhua Hospital, Shanghai Jiao Tong University School of Medicine

Background/aims:
Placental 11β-hydroxysteroid dehydrogenases (11β-HSD1, 11β-HSD2) modulate fetus' exposure to maternal glucocorticoids. Gestational diabetes mellitus (GDM) "programs" an elevated risk of obesity in the offspring. We sought to determine whether placental 11β-HSDs are altered in GDM and the association with metabolic health in early childhood.

Methods:
In a nested matched study of 185 pairs of GDM and euglycemic pregnancies in the Shanghai Birth Cohort, we measured placental 11β-HSD1 and 11β-HSD2 levels, cord blood cortisol and cortisone concentrations, and correlated to adiposity indicators and blood pressure in children at age 4 year.

Results:
Comparing GDM versus euglycemic pregnancies, placental protein levels of 11β-HSD1 (Mean±SD in ratio to β-actin: 0.69±0.31 vs. 0.67±0.31, adjusted p=0.45;) and 11β-HSD2 (0.50±0.21 vs. 0.47±0.19, adjusted p=0.36) were similar, but cord cortisol/cortisone ratios (Mean±SD 1.13±.0.53 vs. 1.26±0.74, adjusted p=0.031) were lower. Higher body fat mass and percent body fat were observed at age 4 years in children of GDM vs. eugylcemic mothers, while there were no differences in systolic and diastolic blood pressures. Placental 11β-HSD2 was weakly positive correlated with children systolic blood pressure. Adjusting for maternal and child factors, one unit increment in placental 11β-HSD2 was associated with a 4.21(95% CI
0.01, 8.42) mmHg increase in child systolic blood pressure.

Conclusions:
Placental 11β-HSD1 and 11β-HSD2 levels were not altered in GDM. Unexpectedly, higher placental 11β-HSD2 levels could be prognostic of higher systolic blood pressure in early childhood.

Funding:

Key-words: (up to 5):
Placental 11β-HSDs, GDM, blood pressure, early childhood

Abstract #00004494 en

The inverse association between prenatal bisphenol A exposure and child atopic dermatitis and other allergic diseases in the first 2 years of life

Impact of Early Life Exposures and Environmental Pollutants

Ouyang Fengxiu (1), Wang Xia (2), Shen Lixiao (2), Zhang Hui-Juan (3), Wang Weiye (2), Luo Zhong-Cheng (4)
(1) Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, (2) Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, (3) The International Peace Maternity and Child Health Hospital, Shanghai Jiao Tong University, (4) Mount Sinai Hospital, University of Toronto, Toronto

Background/aims:
In utero exposure to bisphenol A (BPA) may affect fetal immune system and potentially alter susceptibility to atopic dermatitis and other allergic diseases in later life. However, research data in early life are limited and inconsistent.

Methods:
This study included 334 mother-child pairs from the Shanghai Obesity and Allergy Cohort. Urinary BPA concentrations of mothers at the third trimester and children were assessed using liquid chromatography-tandem mass spectrometry. Four types of allergic diseases, including atopic dermatitis, food allergy, wheezing and allergic rhinitis were ascertained by study dermatologists and pediatricians at postnatal age 12 and 24 months. Logistic regression was applied to estimate the odds ratios (OR) of atopic dermatitis and other allergic diseases.

Results:
A total of 208 infants and toddlers who had at least one of the four types of allergic diseases among whom 186 (89.4%) had atopic dermatitis, and 75 (36.1%) had other allergic diseases. Adjusting for covariates, children in the highest tertile in maternal BPA concentrations had a lower risk of atopic dermatitis at 0-12 months (adjusted OR=0.52, 95%CI: 0.29-0.93) and 12-24 months (adjusted OR=0.22, 95%CI: 0.08-0.61). Similar inverse associations were observed for maternal BPA in relation to the risk of other allergic diseases in children, although they did not reach statistical significance.

Conclusions:
We observed an unexpected inverse association between prenatal BPA exposure and risks of atopic dermatitis and other allergic diseases in infants in the first 2 years of life, suggesting a “protective” impact of prenatal BPA against atopic dermatitis in the offspring.

Funding:

Key-words: (up to 5):
Bisphenol A (BPA), Prenatal exposure, Atopic dermatitis, Allergic disease, Infant

Abstract #00004498 en

The threat of plastic: Effects of maternal exposure to phthalates and nanoplastics on gestational and placental integrity

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Magosso Natalia (1), Vieira de Souza Patrick (1), Franco Moreira Mirella (1), Aguiar Rocha Vanessa (1), Naia Fioretto Matheus (1), Annibal Barata Luisa (1), Fávaro Isabella (1), Cristina Pinha Victória (1), Aquino de Souza Maia Gabriel (1), Rodrigo Scarano Wellerson (1)

(1) Institute of Biociences, Sao Paulo State University (UNESP), Botucatu, SP, Brazil

Background/aims:

The placenta is crucial for healthy fetal development regulating the transfer of nutrients and substances from the mother to the fetus. Phthalates, endocrine-disrupting chemicals, used as plasticizers in plastic products, and nanoplastics (NPs), formed from plastic degradation, are widespread pollutants that contaminate the environment. Both can cross the placental barrier, with NPs potentially carrying phthalates and enhancing reproductive toxicity. This study investigated the effects of gestational exposure to a phthalate mixture (PM) and nanoplastics (NPs), focusing on maternal and placental outcomes.

Methods:

Pregnant rats (CEUA 1174020523) were randomly assigned to six groups: CTR: control; vehicle; T1:20µg/kg/day PM; T2:200mg/kg/day PM; T3:1mg/kg NPs (100nm); T4:20µg/kg/day PM+1 mg/kg NPs; T5:200mg/kg/day PM+1mg/kg NPs. Treatments were administered orally from gestational day 5 (GD5) to GD20. On GD20, 6-8 pregnant rats per group were anesthetized for maternal evaluations. All fetuses were collected and weighed. Placentas were collected for histological (picrosirius red staining) and molecular analysis (RT-qPCR and WB). Data were analyzed using ANOVA followed by Tukey's post hoc test ($p \leq 0.05$).

Results:

There was an increase in pre-implantation loss in T3, T4 and T5 groups vs. CTR and a reduction in fertility potential in T3 group vs. CTR. Additionally, a reduction in male placental weight and an increase in placental efficiency in T3 vs. CTR were observed. The T3 offspring showed a lower number of fetuses appropriate for gestational age (AGA), and T5 a higher number of fetuses small for gestational age (SGA) vs. CTR. Increase in the gene and protein expression of VEGF and IGF-1 in T3 and T4 as well as in collagen quantity in T3-male placentas were observed. Furthermore, a reduction of collagen in T5-female placentas vs. CTR was observed.

Conclusions:

These findings suggest that plastic waste, particularly nanoplastics, altered fertility potential and implantation success, as well as placental growth factors expression and extracellular matrix composition.

Funding:

CAPES (824314/2023-00) and FAPESP (2022/12304-3)

Key-words: (up to 5):

Placenta, nanoplastics, phthalates, maternal health.

Abstract #00004513 en

The impact of prenatal infection on long-term child development

Big Data and Cohorts in DOHaD Research.

Nitschke Amanda (1), Bone Jeffrey (2), Turvey Stuart (3), Lisonkova Sarka (1), Oberlander Tim (3), Hanley Gillian (1)
(1) Department of Obstetrics & Gynecology, University of British Columbia , (2) BC Children's Hospital Research Institute, University of British Columbia, (3) Department of Pediatrics, University of British Columbia

Background/aims:
Prenatal infections have been identified as a risk factor for neurodevelopmental disorders in children. However, little is known about their impact on more nuanced and holistic measures of child development, particularly subclinical symptoms. This study examined the association between maternal prenatal infections and children's socioemotional, language and communication, cognitive development, and physical health at kindergarten (5 years).

Methods:
This population-based retrospective cohort study included all children born in British Columbia between 2000 and 2017 with complete Early Development Instrument outcome data (n=206,491). Children were followed until December 2022. Logistic regression models assessed associations between prenatal infections and developmental outcomes, stratified by trimester, infection site, and infectious agent. A sensitivity analysis restricted the exposure to infections diagnosed during hospital admissions to evaluate the impact of infection severity. Ethics was approved by the UBC Behavioural Research Ethics Board (BREB# H24-02067).

Results:
Prenatal infection was significantly associated with developmental vulnerabilities across multiple domains, including social, cognitive, communication, and physical health (adjusted odds ratios [aOR] ranging from 1.05 [95%CI 1.01-1.10] to 1.09 [95%CI 1.05-1.14]). Associations were more pronounced for first-trimester infections and those of genitourinary or bacterial origin. Infections diagnosed during hospitalization showed the strongest associations, particularly for physical health (OR 1.31 [95%CI 1.15-1.49]), communication and general knowledge (aOR 1.28 [95%CI 1.11-1.48]), language and cognition (aOR 1.26 [95%CI 1.08-1.46]), social competence (aOR 1.25 [95%CI 1.10-1.43]), and emotional maturity (aOR 1.25 [95%CI 1.09-1.42]).

Conclusions:
Prenatal infections were associated with a broad range of developmental vulnerabilities at kindergarten, particularly when infections were more severe and required hospitalization. These findings highlight the importance of further research into the role of maternal immune activation in fetal development and long-term child outcomes.

Funding:
Canada Graduate Scholarships Doctoral Award, Canadian Institutes of Health Research

Key-words: (up to 5):
Big Data, prenatal infection, maternal immune activation, long-term child development

Abstract #00004519 en

Machine Learning to Assess Cutaneous Leishmaniasis Risk Factors in Brazil

Public Health Policies Across the Life Cycle.

Costa de Souza Bruna (1), do Socorro Carvalho Miranda Claudia (1), Veiga Gonçalves Nelson (2), Rossy de Brito Silvana (3)

(1) Institute of Health Sciences, Pará Federal University, Belém, Pará, Brazil, (2) Laboratory of Epidemiology and Geoprocessing of Amazon, University of the State of Pará, (3) Cyberspace Institute, Federal Rural University of Amazon, Belém, Pará, Brazil

Background/aims:

Cutaneous Leishmaniasis (CL) is an infectious disease transmitted by female phlebotomus mosquitoes infected with the protozoan Leishmania spp. Despite a significant reduction in the number of cases in recent decades CL remains a serious public health problem in the Americas, especially in Brazil, which has historically suffered from major socio-economic inequalities and alterations to its natural landscape. Given the above, this study analyzed the occurrence of CL in Brazil and its relationship with socioeconomic and environmental risk factors from 2016 to 2024.

Methods:

This exploratory study used epidemiological, environmental and socioeconomic secondary data obtained from public and official Brazilian government databases and was exempt from approval by a research ethics committee. Descriptive statistics were carried out. The dataset was then divided into 30% for training and 70% for testing and submitted to the random forest Machine Learning (ML) algorithm. After initial analysis, the permutation importance method was applied, as well as estimating the model's performance using the R^2 determination coefficient.

Results:

138,620 cases were analyzed in Brazil, with a higher occurrence in men (73.19%), brown people (65.53%) and those with up to primary schooling (44.99%). Analysis of the database using ML showed the following order of importance of the variables on the occurrence of the disease: Education (1.65), Income (0.75), longevity (0.35) and deforestation (0.30). Evaluation of the performance of the model used showed an R^2 of 0.584.

Conclusions:

The results obtained reinforce the presence of CL in the list of neglected diseases and the existence of an association between its occurrence and socioeconomic and environmental vulnerability in Brazilian territory. The model used was satisfactory for explaining the relationship. It is therefore necessary to develop integrated public policies to mitigate the occurrence of this disease, which consider all aspects of the human, animal and environment relationship, in accordance with the guidelines of one-health.

Funding:

Key-words: (up to 5):

Cutaneous Leishmaniasis; Machine Learning; Data Mining; Epidemiology; Public Health.

Abstract #00004520 en

Early life socio-environmental factors associated with emotional-behavioural problems in childhood and adolescence: a South African birth cohort study

Big Data and Cohorts in DOHaD Research.

Pham Cindy (1), Brink Lucy (2), Springer Priscilla (2), Oakley Bethany (1), Odendaal Hein (2), Potter Mandy (2), Mackay Wendy (2), Smit Petrusa (2), Du Plessis Carolina (2), Khouja Jasmine (3), Wagner Marcelle (2), Pini Nicolo (4),
Sigurdardottir Julie (1), Fifer William (4), Munafo Marcus (3), Murphy Declan (1), Loth Eva (1)
(1) King's College London, (2) Stellenbosch University, (3) University of Bristol, (4) Columbia University

Background/aims:
Approximately 90% of the world's children live in low-middle-income countries (LMIC). Socio-environmental factors influence the pathogenesis of emotional-behavioural problems (EBP; i.e., externalising and internalising problems) in high-income countries studies and are more prevalent in LMIC. Yet, determinants of EBP are largely unknown in LMIC. We investigated the prospective associations between early-life (pregnancy to one-year postnatal) socio-environmental factors and EBP in South African children/adolescents.

Methods:
Data were drawn from the South African-Safe Passage Study; an inception prospective birth cohort study of 7,110 mother-infant dyads with an antenatal sampling frame followed until 1-year postnatal (2007-2016). The AIMS-2-TRIALS-Biomarkers of Neurodevelopmental Outcomes (BONO) follow-up study re-assessed 1,284 caregiver-child dyads at age 5-16 years (2020-2025). Early-life socio-environmental factors (n=398) were collected by questionnaires and/or clinical assessment in the inception cohort. EBP were assessed using the Strengths and Difficulties Questionnaire (SDQ) in BONO. Prospective associations between early-life factors and EBP were examined using linear regression models, adjusted for child's sex and age at SDQ assessment.

Results:
Of the early-life factors, 76 factors (19%) were weakly-moderately correlated (r=-0.20 to 0.43) with one/both EBP outcomes. Maternal psychosocial (e.g., depression, anxiety), lifestyle (i.e., tobacco smoking, alcohol consumption and recreational drug use) and physical health factors (e.g., infections, asthma) during pregnancy, placental abruption and infant food insecurity were associated with both increased externalising and internalising problems. Infant passive smoking was associated with externalising, while informal housing, wheeze and cord length were associated with internalising problems.

Conclusions:
Early-life socio-environmental factors, particularly maternal lifestyle, psychosocial and physical health during pregnancy, may be important predictors of later EBP in children and adolescents and most are modifiable. This foundational work provides the next steps to examine the combined impact of multiple socio-environmental exposures and to elucidate common mechanisms for early detection and preventative strategies of EBP.

Funding:
Innovative Medicines Initiative 2-Joint Undertaking #777394.

Key-words: (up to 5):
Early life, Socio-environmental factors, Emotional-behavioural problems, South African children and adolescents, South African birth cohort study.

Abstract #00004521 en

Maternal COVID-19 infection in pregnancy alters outgrowth and morphology of fetal umbilical cord blood derived endothelial progenitor cells

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Steiner Andreas (1), Kulovic-Sissawo Azra (1), Jaeger Gabriele (1), Weiser-Fuchs Marie-Therese (1), Amtmann Bettina (1), Weiß Elisa (1), Hiden Ursula (1)
(1) Medical University of Graz

Background/aims:
Maternal immune activation by viral infections in pregnancy increases the risk for cardiovascular disease in the offspring. However, the impact of maternal SARS-CoV-2 (COVID-19) infection on fetal endothelial cells remains unclear. Endothelial progenitor cells (EPCs), a pool of circulating cells that grow out as mature endothelial cells and support vascular growth and repair, reflect endothelial function and can be isolated from umbilical cord blood.

Methods:
We isolated fetal, umbilical cord blood derived EPCs (cbEPCs) after healthy pregnancies (control, n=10) and after pregnancies affected by maternal COVID-19 infection (COVID-19, n=9) between gestational weeks 16 and 36, and investigated outgrowth, cellular morphology (microscopic assessment by blinded observers), endothelial barrier function (electric cell-substrate impedance sensing, ECIS), metabolic activity (MTS assay) and proliferation (BrdU incorporation assay). To evaluate inflammatory responses, control and COVID-19 cbEPCs were stimulated with tumor necrosis factor alpha (TNFα).

Results:
COVID-19 exposed cbEPCs showed faster initial outgrowth, exhibited a more elongated shape and swirly monolayer morphology than control cells. TNFα stimulation for 24 h induced a more elongated morphology with swirly growth pattern in control and COVID-19 exposed cells. Notably, TNFα-treated COVID-19 cbEPCs exerted strongest changes in phenotype, while unstimulated COVID-19 cbEPCs resembled morphology of TNFα-treated controls. Further functional analyses (ECIS, MTS, BrdU) revealed no differences between the two groups.

Conclusions:
Maternal COVID-19 infection in pregnancy altered morphology of cbEPCs similar to control cells stimulated with TNFα and lead to a faster outgrowth, suggesting a pro-inflammatory state of the cells. These alterations may have long-term implications for offspring endothelial function.

Funding:
This research was partly funded by the PhD program Molecular Medicine (MolMed) of the Medical University of Graz.

Key-words: (up to 5):
pregnancy, COVID-19, umbilical cord blood, endothelial progenitor cells, cell morphology

Abstract #00004532 en

The Impact of Chronic Mild Maternal Stress Before and During Gestation on Offspring Development and Health

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

de la Cruz Borthiry Fernanda Luz (1), Beltrame Jimena S (1), Cañumil Vanesa A. (1), Krawczyk María C (2), Medina Candela (2), Negri Malbrán Mercedes (3), Boccia Mariano (2), Boccia Mariano (2), Leguizamón Gustavo (3), Franchi
Ana M (1), Ribeiro María L (1)
(1) Laboratorio de Fisiología y Farmacología de la Reproducción, CEFYBO (UBA-CONICET), (2) Laboratorio de Neurofarmacología de los Procesos de Memoria, Cátedra de Farmacología, FFyB, UBA, (3) CEMIC-CONICET, Sección Medicina Materno fetal, Departamento de Obstetricia y Ginecología

Background/aims:
Background: The uterine environment plays a crucial role in fetal and offspring development. We observed that exposing female mice to chronic mild maternal stress results in metabolic changes in the mother and alterations in the vascular adaptations and immunological balance of the maternal-fetal interface. Moreover, fetuses exhibited lower weight.
Our goal is to evaluate the impact of these maternal changes on the development and health of the offspring.

Methods:
Methods: Female BALB/c mice were exposed to a chronic mild stress protocol for two weeks before mating, and continued until term labor. Afterward, all mothers and pups were housed in control conditions. The stress stimulus consisted of reduced bedding material and a shaking protocol that lasted one minute every other day. Pups were weighed weekly, developmental milestones were assessed, metabolic parameters in serum were analyzed, and cognitive and behavioral tests were performed.
The study was approved by the CICUAL of the School of Medicine, UBA (Nº2021-1725).

Results:
Results: We observed that pups from stressed mothers presented a lower birth weight, which persisted until postnatal day 42. Additionally, offspring from stressed mothers showed delayed developmental milestones like tooth eruption, eye opening, and pinna detachment. Six-week-old male pups from stressed mothers exhibited elevated triglyceride serum levels, while female pups presented lower total cholesterol serum levels and fat deposits.
Finally, behavioral differences were observed between male pups of the experimental groups in the passive avoidance and open field tests.

Conclusions:
Chronic mild stress before and during pregnancy affects fetal development, impacting pup growth, metabolism, and behavior later in life. These findings underscore the importance of a healthy maternal environment for optimal offspring development.

Funding:
FONCyT (PICT 2021 N°0221) and CONICET (PIP 2022-2024 N°0100950). The funders had no role in the study design, data collection, or analysis.

Key-words: (up to 5):
chronic mild maternal stress, gestation, developmental milestones, offspring metabolism

Abstract #00004543 en

Maternal diabetes led to increased markers of a proinflammatory and profibrotic state in the postpartum dam´s heart: Effects of a maternal diet enriched in olive oil.

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Taylor Virginia (1), Gatti Cintia Romina (1), Schibert Florencia (1), Higa Romina (1), Jawerbaum Alicia (1) (1) CEFyBO, CONICET-UBA

Background/aims:
Diabetes in pregnancy causes short- and long-term complications in both mothers and offspring. Previously, we found that a maternal diet enriched in extra virgin olive oil (EVOO) prevented long-term impairments in the heart of the offspring. Aim: to evaluate whether an EVOO-enriched diet ameliorates proinflammatory/profibrotic markers in the heart of diabetic dams at postpartum.

Methods:
A mild pregestational diabetic rat model was induced by neonatal administration of streptozotocin (90 mg/kg sc). Control and diabetic females, mated with healthy males, were fed with diets enriched or not with 6% EVOO during pregnancy. The hearts of the dams were collected one-month postpartum (CICUAL RES-4081/04/22). Expression of genes related to the proinflammatory (TNFα and MMP9) and the profibrotic (FGF21, TGFβ1 and CTGF) status was measured by qPCR. Levels of miR-21 and miR-155, related to the proinflammatory/profibrotic state when overexpressed, were measured by stem-loop qPCR. Statistical analysis: one-way ANOVA, n=6-8.

Results:
The heart of diabetic dams showed increased mRNA expression of TNFα and MMP9 (2.38- and 4.54-fold, respectively, $p<0.05$ vs. controls). Increased expression of FGF21, TGFβ1 and CTGF was found in the heart of diabetic dams (3.29-, 1.47- and 1.81-fold, respectively, $p<0.05$ vs. controls). Alterations in TNFα and TGFβ1 expression were prevented by the EVOO-enriched maternal diet ($p<0.05$ vs. diabetic group). Levels of miR-21 and miR-155 were reduced in the heart of diabetic dams (0.16- and 0.55-fold, $p<0.05$ vs. controls), alterations that were not prevented by the maternal diet enriched in EVOO.

Conclusions:
Diabetic dams showed increased markers of proinflammatory/profibrotic damage, which occurs despite low levels of miR-21 and miR-155. A maternal diet enriched in EVOO partially ameliorates the proinflammatory/profibrotic state in the heart of diabetic dams at postpartum

Funding:
Foncyt-PICT 2021- N0 00078

Key-words: (up to 5):
Maternal diabetes – long term outcomes – extra virgin olive oil – heart- postpartum.

Abstract #00004544 en

Maternal diabetes programs the dysregulation of PPAR pathways in the decidua of early pregnant offspring of diabetic rats: Effects of a maternal diet enriched with extra virgin olive oil.

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Gatti Cintia Romina (1), Roberti Sabrina Lorena (2), Taylor Virginia (1), Higa Romina (1), Jawerbaum Alicia (1)
(1) Laboratorio de Reproducción y Metabolismo - CEFYBO - CONICET - UBA, (2) Laboratorio de Regulación Génica en Células Madre - IQUIBICEN - FCEN - UBA

Background/aims:
Alterations in PPAR nuclear receptors are programmed in the decidualized uteri of prepubertal offspring of diabetic rats, and are prevented by maternal diets enriched in extra virgin olive oil (EVOO). Aim: To evaluate PPAR pathways and the pro-oxidant state in the decidua of 9-day pregnant offspring of diabetic dams and the effects of a maternal EVOO-enriched diet.

Methods:
Mild pregestational diabetes was induced in F0 rat neonates with streptozotocin (90 mg/kg sc CICUALRes23732017). Control and diabetic females (F0), bred to healthy males, received a 6% EVOO-enriched diet or a standard diet from day 1 of pregnancy until parturition (n=6-8 per group). Female offspring (F1) were fed a standard diet and bred to healthy males at 3 months of age. Decidua were collected on day 9 of gestation. PPAR levels were evaluated by Western blot, microRNAs targeting PPARs by stem-loop RT-qPCR and levels of the lipoperoxidation marker 4-hydroxynonenal levels (4-HNE) by immunohistochemistry.

Results:
Pregnant offspring of diabetic rats showed reduced decidual levels of PPARα, PPARγ and PPARδ (60%, 40% and 51% respectively, $p<0.05$ vs. controls), alterations observed in parallel with increased levels of miR-21, miR-19b and miR-122 (1.92-, 1.56- and 3.23-fold, respectively, $p<0.05$ vs. controls), negative regulators of these respective PPAR isoforms. These alterations were not prevented by the EVOO-enriched diet provided on F0 gestation. Increased decidual levels of 4-HNE were observed in the offspring of diabetic dams (65%, $p<0.05$ vs. controls), an alteration prevented by the EVOO-enriched diet ($p<0.05$).

Conclusions:
Maternal diabetes programs PPARs dysregulation in the decidua of the early pregnant female offspring, an alteration probably related to altered microRNAs targeting these nuclear receptors. Despite PPAR dysregulation, an EVOO-enriched maternal diet was able to prevent increased lipoperoxidation in the decidua of pregnant offspring of diabetic rats.

Funding:
Foncyt-PICT 2020-0933

Key-words: (up to 5):
Maternal diabetes - PPAR - miR - decidua - olive oil

Abstract #00004566 en

Risk factors for mental disorders in pregnant women: A comparison between the Jundiaí and Araraquara cohorts in Brazil

Public Health Policies Across the Life Cycle.

Rondó Patricia (1), Victor Audêncio (1), Leitão Maria Paula (1), Batista Livia (1), Teles Laisla (1), Argentato Perla (1), Luzia Liania (1), Artes Rinaldo (2)
(1) University of São Paulo, School of Public Health, São Paulo, SP, Brazil, (2) Institute of Education and Research

Background/aims:
Mental disorders during pregnancy are a growing public health concern, with potential consequences for maternal and child health. However, little is known about how the risk factors for maternal mental health may change over time due to shifts in the social, economic, and healthcare contexts. This study compares two population-based cohorts from Brazil, 20 years apart, to identify and contrast the key predictors of mental disorders during pregnancy.

Methods:
We analyzed data from the Jundiaí cohort (1997–2000) and the Araraquara cohort (2017–2024), both located in the state of São Paulo. Mental health was assessed using the GHQ-12, STAI (state and trait), and PSS scales at three prenatal visits. We used panel data analysis with random effects to estimate associations between mental health scores and sociodemographic, housing, obstetric, and morbidity-related variables.

Results:
Pregnant women in the Araraquara cohort presented significantly higher scores in anxiety, depression, and stress measures compared to those in Jundiaí. Key risk factors included being single, separated, or widowed; lower income and education; higher household density; and infectious and hypertensive morbidities during pregnancy (urinary tract infections, cervicitis, vaginitis, and tuberculosis). In contrast, higher pre-gestational weight and being employed were associated with lower anxiety scores. Over time, mental health scores tended to improve across pregnancy in both cohorts but remained consistently higher in Araraquara.

Conclusions:
The results underscore the evolving nature of mental health risk factors and the persistent influence of social vulnerability on pregnant women's psychological well-being. Interventions should prioritize the integration of mental health services in prenatal care, especially for women facing social or health-related challenges. Policy efforts must address broader structural inequalities that contribute to poor maternal mental health.

Funding:
Funding: São Paulo Research Foundation-FAPESP (grants 1998/00321-0 and 2015/0333-6).

Key-words: (up to 5):
Keywords: Mental disorders, pregnancy, depression, risk factors, public health.

Abstract #00004567 en

Mental health and gestational weight gain: A comparison between Brazilian cohorts

Big Data and Cohorts in DOHaD Research.

Victor Audêncio (1), Leitão Maria Paula (1), Argentato Perla (1), Batista Livia (1), Teles Laisla (1), Luzia Liania (1), Artes Rinaldo (2), Rondó Patricia (1)
(1) University of São Paulo, School of Public Health, São Paulo, SP, Brazil, (2) Institute of Education and Research

Background/aims:
Maternal mental health is a crucial determinant of pregnancy outcomes, influencing both maternal well-being and fetal development. This study aims to investigate the association between maternal mental health and gestational weight gain (GWG) in two Brazilian cohorts conducted two decades apart.

Methods:
Data were obtained from the Jundiaí (1998–2000) and the Araraquara (2017–2024) prospective cohort studies. Maternal mental health was assessed during three pregnancy periods using the General Health Questionnaire (GHQ-12), the State-Trait Anxiety Inventory (STAI), and the Perceived Stress Scale (PSS). Bivariate analyses (Kruskal-Wallis, chi-square, and Fisher's exact test) and multinomial ordinal logistic regressions were conducted to assess the associations between mental health variables and GWG, adjusting for sociodemographic, obstetric, and behavioural covariates.

Results:
In the Jundiaí cohort, high levels of stress and anxiety were significantly associated with increased odds of insufficient GWG. Specifically, women in the second quartile of PSS scores during the first trimester had reduced odds of insufficient GWG (adjusted OR:0.36; 95%CI:0.18–0.71), suggesting a possible protective effect of mild stress. In the second trimester, elevated trait anxiety (TAI ≥ 40) was associated with higher odds of insufficient GWG (adjusted OR:1.76; 95%CI:1.12–2.76). In the third trimester, high perceived stress (fourth quartile) was again linked to insufficient GWG (adjusted OR:1.72; 95%CI:1.02–2.91). In the Araraquara cohort, no significant associations were found between mental health indicators and GWG, possibly reflecting improvements in access to prenatal care, mental health services, and social protection policies over the past two decades.

Conclusions:
The contrast between the two cohorts underscores how broader temporal and contextual changes, such as expanded public health coverage and increased awareness of maternal mental health, can alleviate the effects of psychological distress on pregnancy.

Funding:
São Paulo Research Foundation-FAPESP (grants 1998/00321-0 and 2015/0333-6).

Key-words: (up to 5):
Maternal mental health, gestational weight gain, prenatal care, psychosocial support, cohort

Abstract #00004581 en

Impact of Intrauterine Exposure to PBDEs on Epigenetic Programming and Lifelong and Intergenerational Health Outcomes: A Novel Meta-Analysis

Impact of Early Life Exposures and Environmental Pollutants

Santos Samaritano Pereira Matheus (1)
(1) Universidade Municipal de São Caetano do Sul

Background/aims:
PBDEs (polybrominated diphenyl ethers) are persistent organic pollutants with high lipophilicity and the ability to cross the placental barrier, disrupting fetal endocrine signaling. Despite widespread industrial use and known toxicity, the epigenetic and intergenerational effects of intrauterine PBDE exposure remain poorly understood. This meta-analysis aimed to investigate, for the first time, the impact of prenatal PBDE exposure on fetal epigenetic mechanisms and its association with long-term and transgenerational health outcomes.

Methods:
Following PRISMA 2020 guidelines, we systematically reviewed observational and experimental studies published between 2000 and 2025 across PubMed, Scopus, Embase, and Web of Science. Inclusion criteria comprised studies evaluating gestational PBDE exposure and specific epigenetic modifications (DNA methylation, miRNAs, histone acetylation), along with metabolic, neurological, and behavioral outcomes. Statistical analysis used a random-effects model (DerSimonian-Laird), heterogeneity was assessed by I^2, and stratified meta-regression by generation (F1 vs F2/F3) was performed.

Results:
A total of 41 studies (n = 58,372 participants) met inclusion criteria. Hypomethylation of MECP2, BDNF, and IL-6 loci was found in 67% of studies. PBDE exposure increased the risk of epigenetic alterations by 185% (RR: 2.85; 95% CI: 1.91–4.12; $p<0.001$; $I^2 = 38\%$). In 42% of studies, these alterations were transmitted to F2/F3 generations. A 71% increase in neurodevelopmental and metabolic outcomes such as ADHD, early-onset obesity, and insulin resistance was observed in F1 individuals with prenatal exposure (RR: 1.71; 95% CI: 1.26–2.22; $p<0.01$).

Conclusions:
This is the first meta-analysis to demonstrate strong evidence that intrauterine exposure to PBDEs induces persistent epigenetic reprogramming with clinical repercussions across generations. PBDEs emerge as silent modulators of biological inheritance, highlighting the urgent need for regulatory actions and environmental surveillance in reproductive health.

Funding:
This study did not receive any external funding.

Key-words: (up to 5):
PBDEs, epigenetics, environmental pollutants, intrauterine exposure, transgenerational

Abstract #00004622 en

Automatic Carnegie Staging of the Human Embryo Using Artificial Intelligence: The Rotterdam Periconception and Generation R Next Study

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Bastiaansen Wietske (1), Graafland Naomi (2), Niemantsverdriet Ruben (2), Vos Frans (3), Jaddoe Vincent (2), Steegers-Theunissen Régine (2), Klein Stefan (2), Rousian Melek (2)
(1) Erasmus MC, University Medical Center, Rotterdam, The Netherlands, (2) Erasmus Medical Center, Rotterdam, The Netherlands, (3) Delft University of Technology

Background/aims:
Human embryonic development occurs in the first 8-10 weeks post-conception, with the 23-stage Carnegie system assessing morphological development during this critical period. We aim to automate Carnegie staging using AI for improved early assessment and monitoring.

Methods:
To develop and validate our AI model, we used 1257 first-trimester 3D ultrasound images from 750 pregnancies from the Rotterdam Periconception Cohort, staged by an expert rater. Internal validation was performed on an additional 100 images from 47 pregnancies, assessed twice by the expert rater and once by a second expert rater to evaluate rater-variability. For external validation, we analyzed 1197 3D ultrasound images from 894 pregnancies from the Generation R Next study, staged by the second rater. We compared multi-class accuracy (MA) and Mean Absolute Error (MAE) between raters and AI across 10 stages: <16, 16–23, and >23.

Results:
The AI model achieved a MA of 74% (95%CI:[65%, 83%]) and a MAE of 0.27 (95%CI:[0.18, 0.36]) during internal validation. These results were comparable to intra-rater results (MA: 75%, 95%CI:[66%, 83%], MAE: 0.25, 95%CI:[0.16, 0.33]) and inter-rater results (MA: 72%, 95%CI:[63%, 80%], MAE: 0.28, 95%CI:[0.20, 0.37]). External validation yielded a MA of 67% (95%CI:[64%, 70%]) and a MAE of 0.37 (95%CI:[0.34, 0.41]).

Conclusions:
Our findings show that AI can automatically determine the Carnegie stage in utero with accuracy comparable to human raters. This automation removes the need for expert assessment, streamlining early monitoring of embryonic morphological development. Parental health and lifestyle factors shape early development and influence the lifelong health of offspring. By incorporating AI, we enhance early assessment, supporting a deeper understanding of how parental health and lifestyle affect long-term health outcomes and opening new possibilities for early detection and intervention.

Funding:
Erasmus MC2 Research Innovation Grant 2022

Key-words: (up to 5):
Carnegie stage, First trimester, Human embryo, Ultrasonography, Artificial Intelligence

Abstract #00004623 en

Maternal thyroid hormones during late pregnancy are associated with offspring coagulation system

Impact of Early Life Exposures and Environmental Pollutants

Zhang Yong (1), Ma Guojun (2), Fan Jianxia (1)
(1) Shanghai Jiao Tong University, (2) Tongji University

Background/aims:
The exact mechanism of hemostasis in thyroid dysfunction has not been fully elucidated. Thyroid function may have a direct or indirect effect on platelet maturation and function, synthesis and activity of coagulation factors as well as altered blood viscosity. We aim to examine whether maternal free thyroxin (FT4) and thyrotropin (TSH) levels in late pregnancy are associated with coagulation parameters in the offspring.

Methods:
A total of 12,909 women with singleton pregnancies in our hospital were enrolled in this study. Each patient provided serum samples for analyses of thyroid function in late pregnancy. Available patient data for analysis included: maternal age, parity, educational levels, maternal anthropometrics, FT4, TSH, thyroperoxidase antibody (TPOAb), activated partial thromboplastin time (APTT), prothrombin time (PT), D-dimer and thrombin time (TT).

Results:
After adjusting for maternal age, BMI, parity, education levels, sex of the fetus and TPOAb titers, FT4 levels were found to be positively correlated with PT (β=0.028, p<0.0001), and inversely correlated with D-dimer (β=-0.026, p=0.003). Additionally, TSH levels were inversely correlated with APTT (β=-0.11, p=0.006) and positively correlated with D-dimer levels (β=0.032, p=0.015). There was no significant association between FT4 and TT as well as TSH and TT.

Conclusions:
Maternal thyroid function in late pregnancy is closely related with APTT, PT and D-dimer measurements.

Funding:
This work was supported by grants from the National Natural Science Foundation of China (82261128001, 81974235); National Key Research and Development Program of China (2018YFC1004602).

Key-words: (up to 5):
Thyroid function, Coagulation, Hemostatic system, Bleed, Hypercoagulability

Abstract #00004625 en

Arachidonic acid-derived dihydroxy fatty acids in neonatal cord blood relate symptoms of autism spectrum disorders and social adaptive functioning.

Big Data and Cohorts in DOHaD Research.

MATSUZAKI HIDEO (1)
(1) Japan / University of Fukui

Background/aims:
Autism spectrum disorder (ASD) is associated with abnormal lipid metabolism, such as a high total ratio of omega-6 to omega-3 in polyunsaturated fatty acids (PUFAs). PUFAs are metabolized to epoxy fatty acids by cytochrome P450 (CYP); then, dihydroxy fatty acid is produced by soluble epoxide hydrolase. This study examined the association between PUFA metabolites in the cord blood and ASD symptoms and adaptive functioning in children.

Methods:
This prospective cohort study utilized cord blood to quantify PUFA metabolites of the CYP pathway. The Autism Diagnostic Observation Schedule (ADOS-2) and Vineland Adaptive Behaviors Scales, Second Edition (VABS-II) were used to assess subsequent ASD symptoms and adaptive functioning in children at 6 years. The analysis included 200 children and their mothers.

Results:
Arachidonic acid-derived diols, 11,12-diHETrE was found to impact ASD symptom severity on the ADOS-2-calibrated severity scores and impairment in the socialization domain as assessed by the VABS-II ($P = 0.0003$; $P = 0.004$, respectively). High levels of 11,12-diHETrE impact social affect in ASD symptoms ($P = 0.002$), while low levels of 8,9-diHETrE impact repetitive/restrictive behavior ($P = 0.003$). Notably, there was specificity in the association between diHETrE and ASD symptoms, especially in girls.

Conclusions:
These findings suggest that the dynamics of diHETrE during the fetal period is important in the developmental trajectory of children after birth. Given that the role of diol metabolites in neurodevelopment in vivo is completely uncharacterized, the results of this study provide important insight into the role of diHETrE and ASD pathophysiology.

Funding:
This work was supported, in part, by KAKENHI from the Ministry of Education, Culture, Sports, Science and Technology of Japan (19K21754 to HM, 22H00492 to KJT). This work was also partially supported by the Life Science Innovation Center, the University of Fukui, and the Center of Developmental Education and Research.

Key-words: (up to 5):
adaptive functioning, arachidonic acid, autism, cord blood, dihydroxy eicosatetraenoic acid.

Abstract #00004629 en

MATERNAL POLYUNSATURATED FATTY ACID STATUS DURING EARLY PREGNANCY AND PRESENCE OF DYSMENORRHEA IN OFFSPRING AT AGE 15-16 YEARS

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Vrijkotte Tanja (1), Zhou Siyu (1)
(1) Amsterdam UMC, department of Public and Occupational Health, location University of Amsterdam

Background/aims:
Dysmenorrhea affects a significant proportion of young women. While the implication of prenatal nutritional factors on children's health is extensively documented, the influence on dysmenorrhea in offspring remains unexplored. The study investigated the association between maternal fatty acid status during early pregnancy and dysmenorrhea in adolescent offspring, with potential mediating role of age at menarche.

Methods:
Data from the Amsterdam Born Children and their Development (ABCD) population-based cohort study (n=626 mother-daughter pairs) were analyzed using multivariable logistic regression analysis with odds ratios (95% CI). Maternal fatty acid profiles were assessed in plasma at the 12th week of gestation and follow-up self-report questionnaires were completed by their daughters aged 15-16. Dysmenorrhea was defined as the presence of painful cramping in the abdomen and/or back during or just before the menstrual phase.

Results:
The prevalence of dysmenorrhea was 84.7%. Adjusting for confounders, results revealed a negative association between total omega-3 fatty acids and dysmenorrhea (OR 0.85; 95% CI 0.73-0.98) and a positive association between the omega-6 to omega-3 fatty acid ratio and dysmenorrhea (OR 1.20; 95% CI
1.01-1.44), with age at menarche fully mediating these relationships.

Conclusions:
In conclusion, higher maternal omega-3 fatty acid status, especially relative to omega-6 fatty acids, are associated with a reduced presence of dysmenorrhea, with later age at menarche playing a full mediating role. These findings underscore the importance of maternal omega-3 fatty acid intake during pregnancy as part of a balanced diet in shaping the health of future generations.

Funding:
Amsterdam University Medical Center

Key-words: (up to 5):
pregnancy fatty-acid-status dysmenorrhea offspring fetal-programming

Abstract #00004630 en

Effect of paternal obesity on cognitive function of male and female adolescent and adult mouse offspring.

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Chadwick Hannah (1), Bambini Junior Victorio (1), Dawson Neil (1), Hawkes Cheryl (1) (1) Lancaster University

Background/aims:
Almost 60% of adults globally are currently estimated to be overweight or obese. Consequently, rates of obesity in expecting mothers and fathers are also significantly high. Elevated maternal pre-pregnancy BMI is associated with increased incidence of autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), and anxiety, as well as deficits in learning and memory in their offspring. Less well explored, however, is the impact of paternal obesity on long-term brain health and function of offspring across multiple phases of brain development. Therefore, this study investigated the impact of paternal high fat feeding on cognitive function in adolescent and adult mouse offspring.

Methods:
Stud C57Bl/6 mice were fed a control (C, 10% fat) or high fat diet (HF, 45% fat) for 6 weeks before mating. Male and female offspring were fed the C diet from weaning, generating two groups of offspring – C/C (N = 27) and HF/C (N = 24). A range of behavioural tests were used to assess spatial memory, attention and compulsivity, anxiety and motor learning at P50 and 6-months of age. All studies were approved by the local AWERB and carried out in accordance with the UK Animals (Scientific Procedures) Act 1986 (PPL1858313).

Results:
No significant differences were noted between adult C/C and HF/C offspring in the Y-maze, nestlet shredding, marble burying or open field testing. However, C/C females showed better motor memory than male C/C mice (P=0.0219), while there was no significant difference between HF/C male and HF/C female mice (P=0.0612).

Conclusions:
Little difference in cognition has been detected between adult HF/C and C/C offspring. Additional analyses of adolescent offspring may reveal a neurodevelopmental impact. Further tissue analysis for neuronal markers may also reveal the impact of paternal obesity on cellular changes, particularly within the motor cortex.

Funding:
Faculty of Health and Medicine at Lancaster University, UK.

Key-words: (up to 5):
Paternal obesity, Neurodevelopmental disorders, Cognition, Behaviour, Learning and memory.

Abstract #00004638 en

The OLIDIAG multicenter study: Maternal diet supplementation with extra virgin olive oil improves perinatal outcomes in gestational diabetes mellitus.

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Jawerbaum Alicia (1), Gorban de Lapertosa Silvia (2), Rey Magdalena (3), Argerich Inés (4), Reynoso Mariano (5), Muntaner María Celeste (6), Bertona Celina (7), Kojdamanian Favetto Verónica (8), Díaz Esteban (9), Sucani Stella (10), Gomez Ribot Dalmiro (1)
(1) CEFYBO CONICET - Facultad de Medicina - UBA, (2) Universidad Nacional del Nordeste, (3) Hospital Aleman, (4) Hospital Perrupato, (5) Cátedra de Biología Celular y Molecular, Depto. de Ciencias Biológicas, FFYB, UBA, (6) Unidad Patagónica de Medicina Materno fetal y Embarazo de Alto riesgo, (7) UNCUYO, (8) CEPA Pilar, Municipalidad de Pilar, (9) Hospital Gral. de Agudos Dr. Ignacio Pirovano, (10) Hospital Materno Provincial Dr. Felipe Lucini

Background/aims:
Gestational diabetes mellitus (GDM) is a prevalent disease associated with adverse maternal, neonatal and offspring outcomes. Dietary supplementation with extra virgin olive oil (EVOO) regulates metabolic parameters and reduces pro-oxidant and pro-inflammatory markers in several diseases. Aim: To study the effects of an EVOO-supplemented diet in patients with GDM on maternal and neonatal outcomes at delivery.

Methods:
We conducted a multicenter, parallel, randomized, controlled intervention trial of EVOO supplementation in GDM patients (ethical approval UNNE58/20). 190 GDM patients were randomized to receive or not receive 3 tablespoons of EVOO daily from enrollment (<29 weeks gestation) until delivery. Data on maternal and neonatal outcomes were collected. Statistical analysis: Fisher´s exact test and ANCOVA.

Results:
There were no changes in maternal glycemia, triglyceridemia and BMI at enrollment in the groups evaluated, although at term, triglyceridemia was reduced in GDM patients receiving the EVOO-enriched diet (-16%, $p<0.01$ vs. non-supplemented group). Regarding maternal outcomes, no significant changes were observed in hypertensive disorders, placental vascular alterations, cholestasis, postpartum hemorrhage, preterm delivery and non-elective cesarean section in the GDM patients receiving or not receiving the EVOO-enriched diet. Regarding neonatal outcomes, there was a reduction in neonatal weight in the EVOO-supplemented group ($p=0.047$, adjusted for gestational age, vs. non-supplemented group). No significant changes were observed in neonatal hypoglycemia, hyperbilirubinemia, respiratory distress syndrome, stillbirth, large for gestational age and small for gestational age. In the group receiving EVOO supplementation, there was a reduction in the risk of neonates with more than one complication (RR 0.86; $p=0.020$) and in the need for neonatal intensive care unit (RR 0.87; $p=0.032$) compared to the non-supplemented group.

Conclusions:
Maternal diet supplemented with EVOO improves maternal hypertriglyceridemia and neonatal outcomes relevant to long-term offspring health in patients with GDM.

Funding:
Sociedad Argentina de Diabetes (SIC2021), Foncyt-PICT-2021-0078.

Key-words: (up to 5):

Gestational diabetes – nutritional intervention – EVOO – maternal and neonatal outcomes.

Abstract #00004639 en

Altered PPAR pathways in the ovary and the decidua from diabetic pregnant dams are related to changes in ovarian microRNAs and regulated by olive oil-enriched maternal diet.

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Schibert Florencia (1), Gatti Cintia Romina (1), Taylor Virginia (1), Capobianco Evangelina (1), Jawerbaum Alicia (1) (1) CEFYBO-UBA, CONICET

Background/aims:
Maternal diabetes impairs decidual function, crucial in fetoplacental development and offspring health. Nuclear receptors PPARs regulate the proinflammatory milieu and are activated by diets enriched in extra virgin olive oil (EVOO). MicroRNAs regulating PPARs produced by the ovary may influence decidual function. Aim: to evaluate the expression of microRNAs that regulate PPARs in the ovary of diabetic pregnant rats, and to address PPARs and proinflammatory markers in the decidua from diabetic animals fed or not with EVOO-enriched diets.

Methods:
A mild pregestational diabetic rat model was induced by neonatal administration of streptozotocin (90 mg/kg sc). Control and diabetic females bred to healthy males, were fed a diet supplemented or not with 6% EVOO during pregnancy. The ovary and decidua were collected on day 14 of pregnancy (CICUAL:5542021). MicroRNAs were evaluated by stem-loop-RT-qPCR; PPAR and IL-6 by RT-qPCR and FABP4 by Western blot. Statistical test: ANOVA, n=7 dams per group.

Results:
The ovary of diabetic rats showed increased levels of miR-27 and reduced expression of its target Pparg (1.76- and 0.71-fold vs. controls, respectively, $p<0.05$), alterations prevented when dams received the EVOO-enriched diet. The ovaries showed increased miR-21 levels and reduced expression of its target Ppara (2.22- and 0.68-fold vs. controls, respectively, $p<0.05$), alterations no longer observed when the dams received the EVOO-enriched diet. In the decidua of diabetic rats, reduced Pparg and Ppara expression (0.44 and 0.53-fold respectively), together with increased Il-6 expression (3.23-fold) and FABP4 levels (+144%), markers of the proinflammatory state, were observed ($p<0.05$ vs. controls), alterations no longer observed when the dams received the EVOO-enriched diet.

Conclusions:
The decidua from diabetic rats showed impaired PPAR pathways and a proinflammatory state, possibly related to ovary impairments, alterations mostly prevented by an EVOO-enriched maternal diet.

Funding:
Foncyt- PICT 2020-0933.

Key-words: (up to 5):
Fetal programming – maternal diabetes – extra virgin olive oil - PPARs.

Abstract #00004640 en

Small Placental Extracellular Vesicles – Potential Mediators of Programming Effects

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Cristian Andreea (1), Fernandez-Twinn Denise (2), Córdova Casanova Adriana (3), Vales Mennitti Lais (2), Pantaleão Lucas (3), Hufnagel Antonia (2), Oyama Lila (3), Aiken Catherine (4), Ozanne Susan (2)
(1) Institute of Metabolic Science & Loke Centre for Trophoblast Research, University of Cambridge, (2) Institute of Metabolic Science - Metabolic Research Laboratories, University of Cambridge, (3) Institute of Metabolic Science – Metabolic Research Laboratories, University of Cambridge , (4) Institute of Metabolic Science & Department of Obstetrics and Gynaecology, University of Cambridge

Background/aims:
Placental-derived small extracellular vesicles (sEVs) and their content have been increasingly recognised as a means of maternal-fetal communication. Moreover, sEVs can travel between tissues and alter metabolism of the target organ, by delivery of sEVs-content (including miRNAs and proteins). This exosomal cargo can be modulated by conditions such as gestational diabetes mellitus and obesity. Using mouse models, we aim to profile the miRNA content of sEVs released by the placenta and explore tissue specificity of placental sEVs uptake.

Methods:
All animal work was approved by the University of Cambridge Animal Welfare Ethical Review Body (AWERB) and was performed according to the UK Animals Scientific Procedures Act 1986. Female C57Bl6/J mice were fed a high-fat high-sugar diet or a chow diet from weaning and throughout pregnancy. At e18.5, murine placentas were collected and cultured as explants for 24h. Placental sEVs were isolated from the explant media using size-exclusion chromatography. Small RNA-sequencing was performed on banked explant-derived sEVs samples. The lowly expressed miRNAs were filtered out by setting a threshold of counts-per-million>10. High throughput microscopy was used to determine the cellular uptake of fluorescently labelled placental sEVs in different cell lines, including embryonic endothelial (C166) and hypothalamic (N46) cells, as well as adult smooth muscle cells (MOVAS).

Results:
We detected 198 miRNAs in the placental sEVs with 8% being modulated by maternal obesity. In vitro analysis showed that the kinetics and magnitude of placental sEVs uptake differed between cell types, with N46 cells demonstrating the greatest uptake.

Conclusions:
These findings suggest that maternal diet is an important modulator of placental sEVs miRNA content. In addition, uptake of these placental sEVs shows cell type specificity with embryonic hypothalamic cells being important targets. This provides a mechanism by which maternal-fetal communication can be modulated by diet and influence fetal health.

Funding:
This work is supported by King's College Cambridge and the Loke Centre for Trophoblast Research through a Loke CTR PhD studentship.

Key-words: (up to 5):
placenta, extracellular vesicles, miRNAs, gestational diabetes, maternal-fetal communication

Abstract #00004658 en

Association of Cardiovascular Health Trajectories Across Childhood and Adolescence with Proteomic Biomarkers in Late Adolescence

Big Data and Cohorts in DOHaD Research.

Aris Izzuddin (1)
(1) Harvard Medical School and Harvard Pilgrim Heath Care Institute

Background/aims:
The American Heart Association put forth the Life's Essential 8 construct (based on 8 health and behavioral factors) to assess cardiovascular health (CVH), which has been shown to strongly predict subsequent cardiovascular disease (CVD) risk. Moreover, the discovery of novel CVD biomarkers has the potential to improve risk-stratification and may inform biological pathways contributing to CVD. However, substantial gaps exist regarding biomarkers that reflect CVH trajectories over childhood and adolescence.

Methods:
Among 420 children (53% female) in Project Viva, we derived CVH scores (range 0-100 points) in early childhood (median age 3.2y), mid-childhood (7.7y), early adolescence (13y), and late adolescence (17.5y), and used segmented mixed-effect models to estimate three sex- and child-specific CVH trajectory parameters: timing of inflection when CVH declines; slope before and after inflection. Using a targeted proteomics approach, we assayed 92 cardiovascular-related proteins from plasma samples collected in late adolescence. We examined associations of CVH trajectory parameters with proteins using linear regression, adjusting for maternal pre-pregnancy body mass index, prenatal smoking, and child age in late adolescence.

Results:
The mean (SD) slope before inflection was 0.6 (1.2) points/y, timing of inflection was 9.1y (1.0), and slope after inflection was -1.2 (0.8) points/y. At a false discovery rate of <0.05, a 1-SD earlier timing of inflection was associated with 33 differentially expressed proteins (DEPs; 15 upregulated, 18 downregulated). A 1-SD slower CVH gain before inflection was associated with 22 DEPs (14 upregulated, 8 downregulated), while a 1-SD faster CVH decline after inflection was associated with 4 downregulated proteins. Pathway analysis showed that 6 proteins were significantly enriched in proteolysis and response to endogenous stimulus pathways.

Conclusions:
Our study identified protein biomarkers reflecting CVH trajectories in children, which may inform risk-stratification approaches and aid in developing prevention strategies to alter CVD progression.

Funding:
American Heart Association 23CDA1050962

Key-words: (up to 5):
Cardiovascular Health; Trajectories; Proteomics

Abstract #00004660 en

Children of overweight and obese fathers have poorer cognitive function in middle age

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Barton Sheila (1), Lin Sharon (1), Hardy Rebecca (1), Godfrey Keith (1), Dawson Neil (1), Hawkes Cheryl (2) (1) , (2) Lancaster University

Background/aims:
Increasing evidence supports a role for paternal obesity on offspring brain health and function. This includes increased risk of neurodevelopmental disorders such as autism spectrum disorder and attention deficit hyperactivity disorder in children born to obese fathers. However, nothing is known about the long-term effect of paternal health on offspring cognition. This study used data from the Framingham Heart Study to determine the impact of paternal body mass index (BMI) on cognitive function in their middle-aged children.

Methods:
The study protocol was approved by Lancaster University Faculty of Health and Medicine Research Ethics Committee (FHMREC19089) and the Institutional Review Board of the Boston University (H-2394). Data were obtained from Generation 2 (Gen 2, parents) and Generation 3 (Gen 3, offspring n=807-1232) participants. Gen 3 cognition was assessed using a neuropsychological battery adapted from the Wechsler Memory Scale-IV. Statistical analyses were carried out using linear mixed modelling with random intercept for families, with Benjamini-Hochberg correction for multiple comparisons.

Results:
Gen 3 participants (mean age = 47.9 years) born to fathers who were overweight or obese in the year of their birth had significantly lower scores on verbal fluency ($p = 0.03$), logical memories ($p= 0.01$) and visual reproduction ($p = 0.01$) tests, compared to offspring of fathers with healthy weight BMI. This relationship was maintained after adjustment for paternal socioeconomic position as well as Gen 3 age, sex and measures of health. Although Gen 3 born to mothers with BMI > 25 were more likely to be obese and have elevated blood pressure and fasting blood glucose, Gen 3 cognition was not affected by maternal BMI.

Conclusions:
Middle aged children born to overweight or obese fathers performed worse on a range of cognitive tests. This suggests that paternal health may have negative long-term consequences for offspring brain function.

Funding:
Alzheimer’s Research UK

Key-words: (up to 5):
Paternal obesity, middle aged children, Framingham Heart Study, cognition

Abstract #00004662 en

The allostatic overload in pregnancy during the COVID-19 pandemic and potential effects on the health of mother-child dyad: A study protocol.

Big Data and Cohorts in DOHaD Research.

Benavente Noelia (1), Huerta Patricia (2), Teillier Fernando (2), Sepúlveda Aldo (2), Urrea Susan (2), Cheuquelao Javiera (2), Castro Patricio (2), Vergara Pablo (3), Enrique Guzmán (2), Escudero Carlos (4), González Marcelo (2)
(1) University of Concepción, (2) Universidad de Concepción, (3) Universidad del Desarrollo, (4) Universidad del Bío-Bío

Background/aims:
Stress exposure during pregnancy, exacerbated by the COVID-19 pandemic, can result in allostatic overload (AOL), a pathophysiological imbalance impacting long-term health. Chile was highly affected by the COVID-19 pandemic, but there are no studies about AOL in pregnant women during this period. This study investigates how AOL during gestation influences maternal cardiovascular health, child neurodevelopment, and mother-child bonding quality in a pandemic context.

Methods:
A historical cohort study design is proposed, examining pregnant women during the pandemic (2020-2021), with a simultaneous mixed methods approach to evaluate the exposure. AOL will be assessed retrospectively via clinimetric surveys and narrative interviews, complementing prenatal mental health evaluations. Cardiovascular parameters (mean arterial pressure and electrocardiogram) and plasma biomarkers (endothelin-1, von Willebrand factor, asymmetric dimethylarginine, among others) of mothers, and children's development and learning status (TADI test) will be evaluated. Primary outcomes include maternal ischemic heart disease incidence, endothelial dysfunction, child neurodevelopmental disorders, and mother-child relationship alterations. Multivariable and machine learning analyses will determine associations between exposure and outcomes.

Results:
We expect to determine higher AOL in pregnant women during the pandemic's first wave, compared to the later period. Also, higher risks of chronic hypertension, endothelial dysfunction, ECG alterations, heart rate variability, child neurodevelopmental disorders, and disturbances in the mother-child relationships in dyads affected by AOL are anticipated. Using a mixed-method approach, we aim to gain a comprehensive understanding of pregnancy in the context of a pandemic, including emergent factors of stress not assessed by quantitative instruments.

Conclusions:
The allostatic overload during pregnancy in the COVID-19 pandemic context may have long-term detrimental effects on maternal and child health. The study design and results could be helpful for the national health system and further protocols to mitigate these risks.

Funding:
FONDECYT Regular #1241905 (ANID, Chile).

Key-words: (up to 5):
Allostatic Load, Pregnancy, COVID-19, Cardiovascular Health, Neurodevelopment.

Abstract #00004690 en

Timing-specific effects of prenatal alcohol exposure on depressive symptom trajectories across childhood and adolescence

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Law Ka Ying Toby (1), Kwong Alex S. F. (2), Lussier Alexandre A. (3)
(1) Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA, USA, (2) Division of Psychiatry, Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK, (3) Department of Psychiatry, Harvard Medical School, Cambridge, MA, USA

Background/aims:
Prenatal alcohol exposure (PAE) can cause negative physiological, psychological, and behavioral outcomes across the lifespan, falling under the umbrella of fetal alcohol spectrum disorder (FASD). People with FASD have disproportionately high risk for mental health diagnoses, with ~50% experiencing depression. As fetal physiological systems develop at varying gestational ages, there may be sensitive periods where prenatal exposures exert stronger effects on mental health outcomes. Of interest, it remains unknown if PAE timing is linked to specific trajectories of depression later in life. Here, we investigated whether sensitive periods for PAE shape the progression and severity of depressive symptoms across childhood and adolescence.

Methods:
We used data from the Avon Longitudinal Study of Parents and Children (N=6,888). Maternal-reported alcohol consumption during pregnancy trimesters (<18w, 18-32w and >32w gestation) were recategorized into no, low, and high PAE (0, 1-7, and 7+ drinks/week, respectively). Using Growth Mixture Modelling in Mplus, we constructed latent trajectories of child internalizing symptoms measured by the Strength and Difficulties questionnaire between ages 4-16.5 years. We conducted multinomial logistic regressions to identify PAE timing and dosages that increased risk for higher depression trajectories, relative to stable, low symptoms.

Results:
We derived 5 distinct depressive symptom trajectories – stable low, progressive increase, moderate childhood peak, high early childhood, and early adolescent peak. High PAE in the second and third trimesters carried 1.8 times (CI=[1.12,3.01], p=0.0133) higher relative risk of being in the progressive increase trajectory, where depressive symptoms rose exponentially into adulthood.

Conclusions:
The impact of PAE on childhood and adolescent mental health outcomes was more pronounced when higher exposure occurred in the second or third trimester. These potential sensitive periods could help identify children at elevated risk for clinical depression, particularly amongst those without a formal FASD diagnosis.

Funding:
National Institute of Alcohol Abuse and Alcoholism #R21AA030640

Key-words: (up to 5):
prenatal alcohol exposure, depression, mental health, growth mixture modeling

Abstract #00004702 en

Mode of birth shapes the development of the gut microbiome in male Wistar rats

Interventional strategies to prevent late-life outcomes resulting from early-life insults

da Silva Araujo Santiago Marcella (1), Nogueira da Silva Lais (2), Medeiros Selegato Denise (3), Mastrorilli Eleonora (3), Werneck de Avellar Maria Christina (2), Zimmermann Michael (3), Elaine Perobelli Juliana (2)
(1) Federal University of Sao Paulo - UNIFESP; European Molecular Biology Laboratory - EMBL, (2) Federal University of Sao Paulo - UNIFESP, (3) European Molecular Biology Laboratory - EMBL

Background/aims:
The gut microbiome, a complex community of microorganisms in the gastrointestinal tract, plays a pivotal role in host development and health. Mode of delivery—vaginal birth or c-section—is a key determinant of early gut colonization; however, the long-term consequences of early microbial alterations remain poorly understood. This study aimed to assess whether c-section affects the developmental trajectory of the gut microbiome composition and metabolome from weaning to adulthood in a rat model.

Methods:
Male Wistar rats were distributed into three groups: VD, vaginal delivered and not cross-fostered; VDCF, vaginal delivered and cross-fostered; and CSCF, c-section delivered and cross-fostered. Cross-fostering (litter exchange) was necessary to mitigate potential interference from the cesarean procedure on lactation. Fecal and plasma samples were collected from all groups at six postnatal days (PND25, 39, 53, 67, 81, 90). Fecal samples underwent untargeted metabolomics at all time points and 16S rRNA sequencing (V4 region) at PND25, 53, and 90. Plasma samples were analyzed by untargeted metabolomics at all time points.

Results:
CSCF animals showed delayed gut microbiome development, with lower alpha diversity over time compared to VD groups. Beta diversity analysis indicated significant shifts in microbial composition in CSCF, especially in adulthood. Genera such as Romboutsia and Limosilactobacillus were more abundant in CSCF animals at weaning and PND 53, respectively. CSCF showed a distinct postnatal trajectory in fecal metabolites compared to VD groups, suggesting unique microbiome-driven development. In contrast, plasma metabolites were more similar across groups, indicating that the observed differences are primarily gut microbiome-specific.

Conclusions:
C-section alters the postnatal developmental trajectory of gut microbiome composition and metabolism, leading to persistent differences compared to vaginally delivered groups. These findings suggest that early-life interventions, such as birth mode, can shape the long-term maturation of the gut microbiome and may have lasting implications for host metabolic health and disease susceptibility.

Funding:
FAPESP (2021/11319-4, 2021/08127-06, 2023/13458-7)

Key-words: (up to 5):
Gut microbiome, Cesarean section, Metabolomics, 16S rRNA, Microbiome development

Abstract #00004746 en

Maternal Swimming Exercise Induces Sex-Dependent Changes in the Expression of Genes Related to Mitochondrial Metabolism in the Cerebellum of Wistar Rat Offspring

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Menegotto M (1), Zanella JV (2), Ilha L (2), Sana PH (2), Vargas SEF (2), Matté C (1)
(1) Programa de Pós-Graduação em Ciências Biológicas - Bioquímica, ICBS, UFRGS, Porto Alegre, Brazil, (2) Departamento de Bioquímica, ICBS, UFRGS, Porto Alegre, Brazil

Background/aims:
Gestational metabolic programming, as proposed by the Developmental Origins of Health and Disease (DOHaD), links early environmental exposures to long-term metabolic outcomes. Maternal physical exercise emerges as a safe and effective strategy for neurodevelopmental modulation. When practiced during pregnancy, exercise is associated with a reduced risk of non-communicable chronic diseases (NCDs) and improved metabolic and neurological development in the offspring. This study investigated the transgenerational effects of maternal exercise during gestation on the expression of genes encoding proteins related to mitochondrial metabolism in offspring neurodevelopment.

Methods:
Adult female Wistar rats underwent five weekly 30-minute swimming sessions, starting one week before mating and continuing throughout gestation. On postnatal day 7 (PND7), offspring were euthanized and cerebellum were collected. Procedures were approved by the UFRGS Animal Ethics Committee (CEUA/UFRGS, protocol #39441). Gene expression of PGC1α, TFAM, MFN2, NRF2, DRP1, and OPA1 was evaluated by RT-qPCR. Western blotting was used to assess the immunocontent of the corresponding proteins and pAMPK/AMPK. Data were analyzed by two-way ANOVA followed by Tukey's test. Statistical significance was set at p□0.05.

Results:
Maternal swimming exercise significantly increased the expression of PGC1α and TFAM in females
($p<0.05$), suggesting enhanced mitochondrial biogenesis. OPA1 and DRP1 expression also increased ($p<0.0001$ and $p<0.001$), indicating alterations in mitochondrial dynamics. Sex-specific differences emerged within the exercise group, with higher OPA1 ($p<0.0001$), NRF2 ($p<0.05$), DRP1 ($p<0.001$), and TFAM ($p<0.015$) expression in females compared to males. No significant differences were observed in protein immunocontent across groups.

Conclusions:
Maternal swimming exercise during gestation induces neuroadaptive effects on the expression of genes encoding proteins related to mitochondrial metabolism in offspring, particularly in females, highlighting sex-dependent modulation of mitochondrial pathways involved in neurodevelopment.

Funding:
Research Support by FAPERGS (PQ 19/2551-0001747-2) and CNPq (PQ2 303377/2021-6).

Key-words: (up to 5):

DOHaD; Maternal Exercise; Mitochondria; Cerebellum; Offspring.

Abstract #00004778 en

Effects of micronutrient supplementation at different stages before and during pregnancy on preterm birth outcomes: A systematic review and meta-analysis

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Salatas Cristal (1), Lawrence Robyn (2), Bloomfield Peter M (1), Alexander Tanith (1), Wall Clare R (1), Bloomfield Frank H (1), Lin Luling (1)
(1) University of Auckland, (2) Massey University

Background/aims:
Preconceptional and periconceptional micronutrient intake may represent critical modifiable factors on maternal and offspring health. We synthesised the existing evidence on the relationship between micronutrient supplementation and food-based sources of micronutrients at different stages before and during pregnancy on PTB risk.

Methods:
We systematically searched 3 electronic databases and 4 registries for randomised controlled trials (RCTs) and quasi-RCTs without restrictions on publication date or language until 19 September 2024. A random-effects model was used to estimate effect sizes as risk ratio (RR) with 95% confidence intervals (CIs) for specific outcomes of interest. Study quality was assessed using the Cochrane Risk of Bias 1 tool, and certainty of evidence was evaluated with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Results:
Data from 142 RCTs involving 223,246 participants were included. Micronutrient supplementation during pregnancy, specifically fish oil or multiple micronutrient (MMN) supplements, significantly reduced the risk of PTB (RR 0.92; 95% CI: 0.88, 0.96) and increased gestational age at delivery (standard mean difference, 0.05 wks.; 95% CI: 0.01, 0.08). Food-based micronutrients had no effect (RR 0.92; 95% CI: 0.80, 1.07]). Initiation of micronutrient supplementation in the first (0.86; 95% CI: 0.82, 0.90) and second (0.8; 95% CI: 0.74, 0.89) trimesters in high-risk women (0.89; 95% CI: 0.81, 0.97) in high/upper-middle-income regions (RR 0.89, 95% CI: 0.82, 0.97) demonstrated a significant effect on reduced PTB risk.

Conclusions:
Fish oil and MMN supplementation during pregnancy reduces preterm birth risk, with strongest effects observed when initiated early in pregnancy among high-risk women in higher-income regions. Future investigations should focus on the interaction between maternal baseline nutritional status and supplementation to inform more precise intervention strategies.

Funding:
None

Key-words: (up to 5):
Preterm birth; Micronutrients; Preconception; Periconception; Pregnancy

Abstract #00004780 en

Incidence and Associated Factors of Anemia during pregnancy in China: a multiple center prospective cohort study

Public Health Policies Across the Life Cycle.

Zhang Xiaosong (1), Wang Xueyin (2), Juan Juan (2), Gao Di (2), Yang Huixia (2) (1) Peking University First Hospital, (2)

Background/aims:

To investigate the incidence and risk factors on anemia during pregnancy in part of China

Methods:

From Oct. 2020 to Jun. 2024, a prospective cohort study were conducted in 13 hospitals form 7 provinces. The pregnancy women with ≥18 years old were recorded geographic information, history of anemia and haemoglobin(HB) test results by APP in 11-13weeks, 24-27 gestational weeks ,32-35 gestation weeks and ≧36 weeks. Univariate and multivariable logistic regression models were used to analysis.

Results:

There were 18427 pregnancy women in the first interview after consent inform in 13 hospitals, only 10985 pregnancy women had HB test in each interview in 11 hospital to analysis. The overall prevalence of anemia during pregnancy was 23.2%. The incidence rate in 24-27weeks, 32-35weeks and 36weeks were 13.8%, 5.8% and 2.2% separately. The overall incidence in the second or third trimester was 20.5%. Risk factors of incidence of anemia were including parity times(1 time:OR=1.23, 95%CI:1.03-1.47;≧2 times:OR=2.06, 95%CI:1.45-2.92), having anemia history before pregnancy(OR=1.78,95%CI:1.42-2.23), having history of anemia in previous pregnancies(OR=1.78,95%CI:1.43-2.23), and family income was 100001-20000 RMB/month. BMI before pregnancy was overweight and obesity could decrease risk of incidence of maternal anemia(BMI=24-27.9: OR=0.66, 0.68, 95%CI:0.58-0.77; BMI≧28: OR=0.74, 95%CI:0.62-0.89).

Conclusions:

Both of prevalence and incidence of anemia in pregnancy were the high in the second trimester. Further attention needs to be paid to those with pregnancy anemia history or a history of anemia,underweight and multiple deliveries women, and screening should be carried out in on time.

Funding:

This work was supported by grants from the Chinese Preventive Medicine Association

Key-words: (up to 5):

Incidence; prevalence; maternal anemia; risk factors

Abstract #00004782 en

Using Mendelian randomization to examine evidence for the adverse transgenerational effect of grandparental smoking and drinking on the birthweight of their grandchildren in the Norwegian HUNT cohort

Big Data and Cohorts in DOHaD Research.

Musa Hanan (1), Brumpton Ben (2), Evans David (3), Moen Gunn-Helen (4)
(1) Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, (2) HUNT Center for Molecular and Clinical Epidemiology, Department of Public Health and Nursing, NTNU , (3) Institute for Molecular Bioscience, University of Queensland, (4) Institute for Molecular Bioscience, University of Queensland

Background/aims:
Adverse exposures in utero, such as maternal smoking and alcohol consumption are known to have negative impacts on offspring. However, it is hotly contested whether adverse intrauterine exposures also elicit long-term effects that persist across generations.

Methods:
We used Mendelian randomization (MR) across three generations in the Norwegian HUNT study to examine whether grandparental smoking and alcohol consumption had causal effects on grandchildren's birthweight. Grandparental exposures were proxied by an unweighted genetic risk score (GRS) constructed from genetic variants associated with either number of alcoholic drinks per week, smoking initiation, or numbers of cigarettes per day (CPD). Our design leveraged all the advantages of the MR method with its robustness against confounding and reverse causality, plus the opportunity to conduct negative control comparisons involving grandfathers vs grandmothers. More than 14,000 genotyped grandparental-parental trios with grandchild's birthweight were included in the analysis across three generations. As a positive control we performed MR analyses on 6006 grandparental-parental trios with parental birthweight. Additionally, we performed observational analysis to show that the know associations between our exposure and birthweight were present in the HUNT cohort.

Results:
As expected, we found that maternal CPD was observationally associated with decreased offspring birthweight. Interestingly this was also the case for maternal grandmother's (but not the other grandparent's) CPD, smoking initiation and alcoholic drinks per day in the case of grandchild's birthweight. Using MR, we found no strong evidence for a causal effect of grandparental alcohol consumption or smoking on grandchild's birthweight. However, grandmaternal GRS for smoking initiation was, as expected, significantly associated with parental birthweight.

Conclusions:
MR provided little evidence for transgenerational effects of smoking and alcohol consumption across three generations, although we cannot rule out small effects.

Funding:
This project is funded by Australian Research Council (Project number: DE220101226) and the Research Council of Norway (Project grant: 325640).

Key-words: (up to 5):
Transgenerational effect, Birthweight, Mendelian Randomization, intrauterine effects, Barker Hypothesis

Abstract #00004789 en

Milk metabolome of Asian elephants: Insights on early-life nutrition for an endangered species

Big Data and Cohorts in DOHaD Research.

Galante Laura (1), dos Santos Diogo João Franco (2), Mikkonen Elisabeth (2), Madan Shobhit (3), Horak Jeannie (3), Stijepic Zorica (3), Demmelmair Hans (3), Vielhauer Andrea (3), Koletzko Berthold (3), Zaw Htet Thi (4), Htut Win (4), Lummaa Virpi (2), Lahdenperä Mirkka (2)
(1) Swansea University Medical School, (2) Department of Biology, University of Turku, (3) Department of Metabolic and Nutritional Medicine, LMU Munich, Medical Center, (4) Myanma Timber Enterprise

Background/aims:
The Asian elephant is an endangered species with more than 25% of its population living in captivity. High maternal rejection and calf mortality in captive environments highlights the need for better understanding the early-life nutritional requirements of this species. Yet data on maternal milk is available on isolated nutrients without an in-depth analysis of the associated metabolome. This translates in inconsistent nutritional solutions for hand-reared calves.

Methods:
We analysed 70 milk samples (collected ethically according to EU guidelines) from 22 semi-captive Asian elephants in Myanmar, through LC-MS and GC-FID. We then measured and compared these results with results from Biocrates MxP Quant 500XL kits.

Results:
The original method quantified 160 compounds, including amino acids, organic acids, fatty acids, acyl-carnitines and phospholipids. The new method quantified 902 compounds, including the aforementioned compound classes and 24 more, such as biogenic amines, hormones, sugars etc. Results from the first approach showed high glutamate (median: 1727.9, (IQR: 1278.4) µmol l−1) and glycine (2541.7(1704.1) µmol l−1) amongst others. These data were confirmed by the new method which also revealed high concentrations of other compounds, including choline (771 µmol l−1), hexose (516 µmol l−1), putrescine (3539 µmol l−1) and hippuric acid (1301 µmol l−1).

Conclusions:
The information obtained through a metabolomic analysis of maternal milk can provide a detailed insight on 1)the profile of biologically active compounds typically received by calves, 2)the physiology of the lactating mammary gland, 3)the maternal diet and 4)the end environmental microbiome calves are exposed to while nursing. Given the demonstrated importance of early-life nutrition and environmental exposures in humans and other animals, comparative research between maternal milk and milk-replacers, beyond single nutrients, seems essential to fully understand nutritional and physiological requirements of offspring and to optimise conservation efforts for endangered species, possibly counteracting current biodiversity loss trends.

Funding:
The European Research Council, Oskar Öflunds Stiftelse, Swansea University Research Wales Innovation Fund, AaltonenFoundation, and the Strategic Research Council within the Research Council of Finland.

Key-words: (up to 5):
One health, milk metabolome, early-life nutrition, metabolomics, big data

Abstract #00004790 en

Cannabinoid exposure alters placental inflammation and tryptophan metabolism: implications for fetal programming

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Staud Frantisek (1), Ghaddar Mohammad Rida (1), Synova Tetiana (1), Al Souki Mia (1), Unal Vildan (1), Karahoda Rona (1), Machacek Miroslav (2), Abad Cilia (1), Portillo Ramon (3)
(1) Charles University, Faculty of Pharmacy , (2) Charles University, Faculty of pharmacy , (3) Charles University

Background/aims:
The increasing use of cannabis during pregnancy raises concerns about potential effects on placental and fetal development. Exocannabinoids such as Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD) may disrupt immune and metabolic signaling at the maternal–fetal interface. This study aimed to examine the impact of cannabinoid exposure on placental inflammation and tryptophan metabolism, using both human placenta-derived models and a rat in vivo model of prenatal THC exposure.

Methods:
Human villous explants and primary trophoblast cells were treated with various concentrations of cannabinoids (THC, CBD, CBG, CBN, CBV) followed by lipopolysaccharide (LPS) stimulation. Cytokine expression was assessed via RT-qPCR and ELISA; NF-κB activation was visualized using immunofluorescence. Separately, pregnant Wistar rats received oral THC (3 mg/kg/day, gestation days 6–21), and fetal/placental tissues were collected at GD21. Expression of genes regulating tryptophan metabolism (TPH1, IDO2, KMO, KAT1, MAO-A/B, SERT, OCT3) was analyzed via qPCR.

Results:
All tested cannabinoids reduced LPS-induced pro-inflammatory cytokine expression (IL6, TNF, IL1B) in explants and trophoblasts. CBD suppressed NF-κB nuclear translocation, independently of CB1, CB2, or TRPV1 receptor signaling. In the rat model, prenatal THC exposure led to reduced fetal and placental weights and dysregulated expression of key tryptophan metabolism genes in both placenta and fetal organs, suggesting disturbed serotonin and kynurenine pathways.

Conclusions:
Cannabinoid exposure attenuates placental inflammation and modulates metabolic pathways central to fetal development. The suppression of immune signaling and disruption of tryptophan metabolism may contribute to altered fetal programming. These findings support the need for caution regarding cannabis use during pregnancy.

Funding:
Supported by the Czech Science Foundation (23-07094S) and the NETPHARM project (CZ.02.01.01./00/22_008/0004607), co funded by the European Union.

Key-words: (up to 5):
Cannabinoids, placenta, inflammation, tryptophan metabolism, fetal programming

Abstract #00004791 en

Long-Term Effects of Exercise during Pregnancy on Maternal and Offspring Metabolic Health: An 8-to 10- year Follow-Up Study

Interventional strategies to prevent late-life outcomes resulting from early-life insults

GUO JIAMEI (1), Zhang Qidi (1), Deng Yu (1), Sun Tianjiao (1), Ning Jie (1), He Yilin (1), Qianshu Pang (1), Wang Shuxian (1), Wen Xin (1), Han Bing (1), Lin Xiufeng (1), Hou Xinnan (1), Wang Tingting (1), kang Xin (1), Han Xinyue (1), Wei Yumei (1), Wang Chen (1), Yang Huixia (1)
(1) Peking University First Hospital Obstetrics and Gynecology Department

Background/aims:
This study aimed to assess the long-term metabolic effects of gestational exercise in overweight and obese women and their offspring 8-10 years post-intervention.

Methods:
We conducted a follow-up study of a randomized controlled trial (RCT) that originally investigated the impact of prenatal exercise on gestational diabetes mellitus (GDM) incidence. Mother-offspring pairs underwent comprehensive metabolic evaluations, including anthropometric measurements, blood pressure assessment, oral glucose tolerance tests (OGTT), insulin release tests (IRT), and lipid profiling.

Results:
Among 118 mother-offspring pairs completing follow-up (exercise group: n=64, 43.3% ; control group: n=55, 35.5%). Compared to controls, mothers in the exercise group demonstrated superior glycemic control, with lower fasting plasma glucose (5.00 [4.61–5.22] vs. 5.08 [4.89–5.52] mmol/L, p=0.015), 2-hour plasma glucose (6.54 [5.64–8.16] vs. 7.17 [6.28–9.70] mmol/L, p=0.031), fasting insulin (9.14 [6.33–14.56] vs. 12.5 [9.45–16.25] uIU/ml, p=0.018), and 2-hour insulin levels (52.85 [39.70–105.75] vs. 100.85 [65.73–149.25] uIU/ml, p<0.001), along with reduced insulin resistance (HOMA-IR: 1.96 [1.46–3.31] vs. 3.00 [2.09–3.95], p=0.01). They also exhibited improved body composition, including lower BMI (27.15±3.25 vs. 29.45±4.24 kg/m², p=0.010), fat percentage (36.31±5.21% vs. 39.03±5.17%, p=0.050), visceral fat area (128.79±40.21 vs. 151.38±38.22 cm², p=0.002). Offspring in the exercise group showed non-significant trends toward lower BMI Z-scores, fasting glucose, and circumference measurements, along with higher HDL levels.

Conclusions:
This longitudinal study provides novel evidence that moderate intensity exercise during pregnancy confers lasting metabolic benefits for overweight/obese mothers, with potential favorable trends in offspring health.

Funding:
National Key Research and Development Program of China [grant number 2021YFC2700700].

Key-words: (up to 5):
Exercise; Obesity; Follow-up; Metabolism;Maternal-offspring

Abstract #00004796 en

Maternal malnutrition dysregulates lncRNAs that control Cyp2b12 expression and contribute to developmental origin of prostate cancer

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Portela Luiz Marcos Frediani (1), Oliveira Jordana Inácio Nascimento (2), Ferreira Marcel Rodrigues (3), Magdaleno Gustavo Daniel Vega (4), Lorente Ana Beathriz Leite (1), Mattos Renato (1), Ribeiro Isabelle Tenori (1), Fioretto Matheus Naia (1), Ribeiro Marcelo Augusto (1), Perez Erika Stefani (1), Baptista Hecttor Sebastian (1), Barata Luisa Annibal (1), Valente Guilherme Targino (3), Magalhães João Pedro (5), Justulin Luis Antonio (1)
(1) Institute of Biosciences, São Paulo State University, Brazil, (2) Faculty of Sciences, University of Ottawa- Canada , (3) Botucatu Medical School, São Paulo State University, Brazil, (4) University of Guadalajara, (5) University of Birmingham, United Kingdom

Background/aims:
The DOHaD concept establishes the association between disease throughout lifespan and with early stages of development. In this scenario, the exposition of dam's rats to maternal malnutrition is associated with impairment in prostate growth during early-life and an increase of prostate cancer (PCa) incidence during ageing. Here, we use multi-omics approaches to identify lncRNAs, mRNAs, miRNAs, and proteins differentially expressed (DE) and seek to create regulatory networks in the prostate during early-life and ageing to associate with the developmental origin of PCa.

Methods:
We performed RNA-Seq, small RNA sequencing, and proteomics of the ventral prostate of control (CTR, offspring of mothers fed 17% protein) and malnourished (GLLP, offspring of mothers fed 6% protein) animals on postnatal day (PND) 21 and 540 (n=4 animals per group/age/technique). We assembled the transcriptome and identified DE mRNAs, lncRNAs, and miRNAs, and in proteomics, we identified DE proteins. We created interaction networks between lncRNAs-miRNAs/mRNAs/proteins and compared the networks formed in early-life and aging, created functional enrichment and ontological term analyses, and identified molecules commonly DE at both ages. We performed RT-qPCR on the VP of the animals to validate the findings.

Results:
A total of 1,489 lncRNAs were identified. At PND21: 14 lncRNAs, 196 DEGs, 15 miRNAs, and 289 DEPs were altered; at PND540: 35 lncRNAs, 279 DEGs, 20 miRNAs, and 68 DEPs. Networks revealed key modules at PND21 (9 lncRNAs + 44 mRNAs) and PND540 (59 lncRNA–mRNA pairs). We predicted 195 lncRNA–miRNA interactions at PND21 (regulating 190 targets) and 675 at PND540 (regulating 150). Functional enrichment at PND21 changes the cell cycle and PND540 to inflammation. Key molecules included Man2a and Cyp2b12 (qPCR-validated: upregulated at PND21, p=0.0123; downregulated at PND540, p=0.0282).

Conclusions:
Our findings show that maternal malnutrition disrupts lncRNA networks, altering Cyp2b12 expression, impairing prostate development, and potentially promoting PCa.

Funding:
FAPESP 2021/00340-2 and 2022/03990-0

Key-words: (up to 5):
DOHaD, lncRNAs, multiomics, prostate cancer, Cyp2b12.

Abstract #00004797 en

Low Birth Weight children's growth in early life and associated factors

Role of Infant and Young Child Feeding Practices on Long-Term Health

Santa Rosa Victor Hugo (1), Strufaldi Maria Wany Louzada (1), Suano-Souza Fabíola Isabel (1), Luna Leonardo Duarte Sobreira (1), Vieira Erika Loureiro (1)
(1) Escola Paulista de Medicina - Universidade Federal de São Paulo (EPM/Unifesp)

Background/aims:
Low birth weight (LBW) is associated with suboptimal growth and increased risk of noncommunicable diseases across the life course. This study aimed to assess growth patterns and associated factors in LBW infants during the first two years of life.

Methods:
This retrospective observational study included 78 children aged up to 24 months, born >1000g and followed in pediatric outpatient clinics in São Paulo's metropolitan area. Weight, length, and head circumference (HC) at birth and follow-up were converted to Z-scores using Intergrowth-21th and WHO standards. Catch-up growth: increase >0.67 Z-score in weight-for-age. Variables analyzed included gestational weight gain, pregestational BMI, small for gestational age (SGA), breastfeeding duration, and age of complementary feeding introduction. Procedures followed ethical standards for human research.

Results:
The children´s mean age at follow-up was 15.9 months; 48.7% were male, 12.8% SGA, and 42% LBW. Among mothers, 37.9% had pregestational overweight and 47% gained adequate gestational weight. LBW infants had significantly lower gestational age (32.2 vs. 39 weeks, $p<0.001$) and higher SGA prevalence (31.3% vs. 0%, $p<0.001$) vs. those ≥2500g. LBW children showed lower mean Z-scores: length-for-age (-0.71±1.27 vs. 0.32±1.45, $p=0.002$), weight-for-age ($p=0.001$), and HC ($p=0.003$). No significant BMI Z-score difference. Catch-up rates: weight (25%), length (19%), HC (34%); 15.6% remained with short stature. Breastfeeding was less common (25% vs. 52.2%, $p=0.020$), and complementary feeding started later (6.7 vs. 5.7 months, $p=0.009$). No associations found between feeding or maternal weight gain and catch-up. SGA status did not modify results.

Conclusions:
LBW infants showed greater anthropometric recovery, yet persistent growth disadvantages. Nutritional and maternal factors were not significantly associated with catch-up in this study.

Funding:
No external funding.

Key-words: (up to 5):
Low birth weight, child growth, catch-up growth, breastfeeding, early nutrition.

Abstract #00004800 en

Maternal stress alters offspring vascular function, lipid and antioxidante profiles: a sex-dependent response

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Nogueira, Anna Beatriz (1), Monnerat, Juliana (1), Manhães, Anna (1), Reis, Maria Luisa (1), Maciel, João (1), Rocha, Helena (2), Mentzinger, Juliana (2), Teixeira, Gabriel (2), Brito, Fernanda (2), Motta, Nadia (2), Lima, Gabriel (2), Nóbrega, Antonio Claudio (2), Rocha, Natália (2), Medeiros, Renata (1)
(1) Departament of Nutrition and Dietetics, Fluminense Federal University, (2) Department of Physiology and Pharmacology, Fluminense Federal University

Background/aims:
Gestational stress induces physiological changes across generations, which is related to increased cardiovascular risk. The study aimed to determine vascular function, lipid profile, and antioxidant parameters in adult male and female rats subjected to gestational stress.

Methods:
Wistar pregnant rats underwent an unpredictable stress protocol (14th-21st day). After birth, offspring were divided into two groups (8 animals/group/sex) and monitored up to 90 days of life: Control(C) and Stress(S). Mothers blood was collected post-lactation for corticosterone analysis. Offspring blood was collected for lipid profile, platelet aggregation and antioxidant analyses, and thoracic aorta was collected for vascular reactivity analysis (concentration-response curve of acetylcholine and phenylephrine). (Ethics Committee 9518170621).

Results:
Stress protocol increased serum corticosterone in stressed mothers (p=0.04). Regarding the offspring, there were no significant differences in body mass between S and C in both sexes. The S females showed an increase in the platelet aggregation (%) induced by ADP ($p<0.05$) and collagen ($p<0.05$). Moreover, S females had lower HDL (p=0.0003) and superoxide dismutase (p=0.016) levels. No significant differences were observed for total cholesterol, LDL, triglycerides and catalase in both sexes. Concerning vascular function, S females showed an increased vasoconstrictor response to phenylephrine (p=0.02), while the S group showed lower vasodilatory responses to acetylcholine reactivity in both sexes (male p=0.04; female p=0.004).

Conclusions:
Gestational stress impaired endothelium-dependent vasodilation, regardless of sex. In females, there was also reduced antioxidant function and HDL cholesterol, and increased platelet aggregation.

Funding:
CAPES, FAPERJ

Key-words: (up to 5):
Unpredictable stress, metabolic programming, sexual dimorphism, endothelial dysfunction

Abstract #00004804 en

Maternal gut Bifidobacterium controls placental endocrine function

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Lopez-Tello Jorge (1), Kiu Raymond (2), Schofield Zoe (3), Dalby Matthew J. (2), van Sinderen Douwe (4), Le Gall Gwénaëlle (5), J Hall Lindsay (2), Sferruzzi-Perri Amanda N (6)
(1) Faculty of Medicine. Autonomous University of Madrid, Spain, (2) Institute of Microbiology and Infection, University of Birmingham, United Kingdom , (3) Gut Microbes & Health, Quadram Institute Bioscience, Norwich Research Park, Norwich, UK, (4) APC Microbiome Institute, University College Cork, Cork, Ireland , (5) Norwich Medical School, University of East Anglia, Norwich, UK, (6) Centre for Trophoblast Research, University of Cambridge, Cambridge, UK

Background/aims:
The gut microbiota plays a crucial role in pregnancy, as maternal metabolism must adapt to optimise nutrient absorption. Recent studies show that gut microbiota, including Bifidobacterium, influences fetal growth and placental development, particularly the transport region, in mice. Aside from the transport of nutrients, the placenta produces a plethora of hormones crucial for maternal support of pregnancy. Building on these insights, we aimed to assess whether maternal Bifidobacterium breve administration affects placental endocrine function.

Methods:
Germ-free mice were either treated with 100µL of B. breve UCC2003 (concentration of 1010CFU/mL) at gestational days 10, 12 and 14 (BIF group, n=6) or 100µL vehicle control solution (GF group, n=5) by oral gavage. Mice were killed on day 16.5 (term ~day 20), and placental endocrine zones (junctional zone, Jz) collected for molecular analysis (qPCR, proteomics and metabolomics).

Results:
No differences were found in the size of the Jz. However, the BIF group exhibited increased expression of Pcdh12 and Hmgcr, along with a tendency for elevated Cyp17a1, both of which encode enzymes involved in steroidogenesis, compared to the GF group. Additionally, BIF upregulated the expression of key hormones involved in immunity and metabolism, such as prolactins (Prl3a1, Prl3b1 and Prl8a8) and pregnancy-specific glycoproteins (Psg17, Psg18, Psg19, Psg21). Proteomic analysis of the Jz identified 431 proteins regulated by BIF, many of which are involved in transcription, cell cycle progression, and metabolic regulation. Moreover, metabolomic analysis revealed that BIF increased the concentrations of lactate and taurine in the Jz. Changes in the Jz were related to improvements in fetal growth and viability.

Conclusions:
Our results offer novel insights into how the gut microbiota can regulate placental function, opening new avenues for novel therapeutic strategies aimed at optimizing pregnancy outcomes and reducing long-term health risks associated with DoHAD.

Funding:
JL-T is currently supported by a CESAR-NOMBELA Fellowship (2023-T1/SAL-GL-28960) from Community of Madrid (Spain).

Key-words: (up to 5):
Microbiota, Placenta, Endocrinology, Probiotics

Abstract #00004820 en

Traditional definitions of rapid infant weight gain are poorly correlated with WHO weight velocity standards

Big Data and Cohorts in DOHaD Research.

Wood Charles (1), Chen Keying (2), Woo Jessica (3)
(1) Department of Pediatrics, Duke University School of Medicine, (2) Department of Population Health, Duke University School of Medicine, (3) Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine

Background/aims:
Rapid infant weight gain (RIWG) is associated with obesity in large international cohorts, yet this definition relies on cross-sectional references that are not intended to be used to monitor weight velocity. This study aims to assess the concordance of RIWG with World Health Organization (WHO) weight velocity standards using real-world clinical data.

Methods:
We included infants born at term from 7/2012 - 12/2022. We calculated WHO weight velocity intervals between birth, 6 months, and 1 year, defining accelerated weight velocity as Z-scores > 2 SD above the mean and calculated weight-for-age Z-score (WAZ) changes, defining RIWG as >0.67 SD increase and very rapid weight gain (vRIWG) as >1.33 SD increase. We used McNemar tests to compare rapid and very rapid weight gain with accelerated weight velocity categories. The study was approved by the Duke Health Institutional Review Board.

Results:
Among 156,785 infants, 6,048 had intervals from birth to 6 months and 8,061 had intervals from 6 months to 12 months. Infants were 45% non-Hispanic White, 20% non-Hispanic black, 14% Hispanic, 4% Asian, and 17% other race and ethnicity. Between birth and 6 months, 2,558 (42%) infants had RIWG and 1,293 (21%) had vRIWG, yet only 12% and 24% of those had accelerated weight velocity, respectively ($p<0.0001$). Between 6 and 12 months of age, 1,993 (25%) had RIWG and 381 (5%) had vRIWG, yet only 38% and 82% of those had accelerated weight velocity, respectively ($p<0.0001$).

Conclusions:
Rapid weight gain categories do not appropriately identify accelerated weight velocity as defined by WHO standards. Although most infants with >1.33 SD increase in WAZ between 6 and 12 months also had accelerated weight velocity, a minority of infants with rapid weight gain in either time interval also had accelerated weight velocity. WAZ changes appear to be poor approximations of true deviations from healthy infant growth.

Funding:
National Institutes of Health K23HD107157

Key-words: (up to 5):
infant weight gain, obesity, EHR

Abstract #00004825 en

Gestational hypothyroxinemia impairs brown adipose tissue function in offspring

Impact of Early Life Exposures and Environmental Pollutants

Regaldiz Alejandro (1), Pacheco Elisa (1), Millaleo Barbara (2), Gallegos Andres (2), Bastías-Pérez Marianela (2), Santos Johana (1), Riedel Claudia (1), Opazo Ma. Cecilia (2) (1)
Universidad Andres Bello, (2) Universidad de las Americas

Background/aims:
Adipose depots are central in maintaining metabolic homeostasis, and adipose dysfunction contributes to obesity. Early life conditions, such as maternal endocrine health during pregnancy, can influence the function of adipose depots in offspring, potentially affecting long-term metabolic outcomes. Previous research has shown that gestational hypothyroxinemia (HTX)—a condition characterized by low maternal thyroxine—negatively impacts white adipose tissue (WAT) and increases susceptibility to diet-induced obesity in offspring. However, the effect of HTX on other adipose depots, such as brown adipose tissue (BAT), remains unclear. This study aimed to investigate the impact of gestational HTX on BAT function in offspring.

Methods:
To assess BAT function, we conducted thermographic imaging of the interscapular BAT (iBAT) depot in C57BL/6 mice, gestated in HTX conditions, at neonatal and adult stages. Additionally, to evaluate the diet-induced response of iBAT, a subset of mice was fed either a Western-like or standard diet for 12 weeks. Thermographic assessments of iBAT were conducted before and after dietary intervention. In addition, relative expression of BAT (UCP1, Bmp8b, and Cidea) and WAT (Leptin and Adiponectin) markers were assessed by RT-qPCR.

Results:
Our findings demonstrate a reduced thermogenic capacity in the iBAT depot of HTX offspring at both neonatal and adult stages. Moreover, HTX offspring exhibited accelerated weight gain and an impaired thermogenic response from iBAT when exposed to an obesogenic diet. These changes were accompanied by decreased expression of BAT markers and increased expression of WAT markers in iBAT samples.

Conclusions:
These results suggest that gestational HTX impairs iBAT function both at baseline and in response to dietary stimuli, thereby contributing to an increased susceptibility to diet-induced obesity in the offspring.

Funding:
UDLA DI-PIR202425, Programa ICM - ANID, ICN09_016, Programa de Formación de Capital Humano ANID – Beca de Doctorado 2024-21242075

Key-words: (up to 5):
gestational hypothyroxinemia, brown adipose tissue, diet-induced thermogenesis, obesity, early life programming

Abstract #00004826 en

Decoding the Placental Origins of Life: consequences for Long-Term Health in the Generation R Study

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

van der Meeren Lotte (1), Van den Berg Anne-Sophie (2), Adank Annemarijne (2), Painter Rebecca (2), Steegers Eric (2), Jaddoe Vincent (3), Gaillard Romy (3), Mulders Annemarie (4)
(1) Department of Pathology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands, (2) Department of Obstetrics and Gynaecology, Erasmus MC, University Medical Center, (3) The Generation R Study Group, Erasmus MC, University Medical Center, (4) Erasmus MC University Medical Center Rotterdam The Netherlands

Background/aims:
Fetal growth restriction is associated with increased risk of cardiovascular diseases in adulthood. Placental weight is positively linked to birth weight and negatively associated with growth and cardiovascular outcomes in later life. However, these last results are inconsistent and consequently the exact role of the placenta for long-term outcomes remains unclear. The aim of this study was to investigate the association between placental weight and childhood growth and cardiovascular health at the age of 9 years old.

Methods:
Embedded in Generation R, a population-based longitudinal cohort in The Netherlands, this study included 3,689 children born between April 2002 and January 2006. Following delivery, information including birth weight and placental weight was collected. During a follow-up visit (9 years of age) the following parameters on childhood growth and cardiovascular health were collected: body mass index (BMI), total fat mass, systolic- and diastolic blood pressure, mean arterial pressure and intima-media thickness and distensibility of the common carotid artery. Linear regression models were constructed and adjusted for confounders (maternal age and BMI at intake, parity, education level, ethnicity, gestational age at birth, birth weight, pregnancy complications, gender and age of the child).

Results:
In the unadjusted model, placental weight was positively associated with BMI, total fat mass, systolic blood pressure and mean arterial pressure. In the final model, placental weight in SDS (SD score) was positively associated with systolic blood pressure (β 0.47 mmHg, 95%CI 0.13 mmHg;0.81mmHg) only. Placental weight as ratio of birth weight in SDS (SD score) was positively associated with systolic blood pressure after full adjustment (β 0.35 mmHg, 95%CI 0.08 mmHg; 0.62 mmHg).

Conclusions:
Placental weight is positively associated with offspring systolic blood pressure at 9 years of age. This provides a foundation for further research of the association of placenta abnormalities and cardiovascular health in later life.

Funding:
None

Key-words: (up to 5):
Placental weight, cardiovascular health, systolic blood pressure, childhood outcomes

Abstract #00004827 en

Early maternal metabolic syndrome better predicts perinatal complications than body mass index or fat mass

Mechanisms Determining Transgenerational Effects of Health and Disease

González-Ludlow Isabel (1), Piña-Ramírez Omar (2), Rodríguez-Cano Ameyalli (1), Tolentino-Dolores Maricruz (1), Rodríguez-Hernández Carolina (1), Estrada-Gutierrez Guadalupe (3), Solis-Paredes Mario (4), Perichart-Perera Otilia
(1)
(1) Nutrition and Bioprogramming Coordination, INPer, (2) Bioinformatics and Statistical Analysis Department, INPer, (3) Department of Immunobiochemistry, INPer, (4) Department of Genetics and Human Genomics, INPer

Background/aims:
Metabolically unhealthy phenotypes in pregnancy and their association with adverse outcomes remain underexplored. This study aimed to predict adverse perinatal outcomes according to maternal metabolic classifications.

Methods:
This study included 159 pregnant women (OBESO* cohort, Mexico, 2017-2024); 62.9% (n=100) with normal weight and 37.1% (n=59) with obesity [pregestational BMI (pBMI); WHO]. Women classified as overweight (25.0-29.9 kg/m²) were excluded. First-trimester fat mass percentage (FM%) was measured by bioimpedance. Metabolic Syndrome (MS) was defined as having 3 or more of the following: glucose alterations (HOMA-IR, insulin, glucose, or HbA1c), excess FM%, high triglycerides, low high-density lipoprotein, or blood pressure (BP) alterations (pregestational hypertension or BP medication). The main outcome was the presence of any complication: hypertensive disorders of pregnancy, small offspring [small-for-gestational-age, low-birthweight, and intrauterine growth restriction], gestational diabetes, and preterm delivery. A balanced logistic regression classifier with an 8-fold cross-validation estimated the median area under the curve (AUC) and interquartile range for each metabolic classification in predicting perinatal complications. All models included maternal age. The Friedman test (post-hoc BH) assessed AUC differences. All participants gave written consent (No. 3300-11402-01-575-17/2024-1-14). *Origen Bioquímico y Epigenético del Sobrepeso y Obesidad

Results:
Maternal age was 29 (18-43); 47.8%(n=76) had MS. In the MS group, more women presented complications (76.3%) compared to the metabolically healthy group (43.4%;p<0.001). No differences were observed in perinatal complications according to obesity status (obesity-pBMI or obesity-FM%).
The median AUC for predicting 1 or more adverse outcomes was significantly higher with the MS classification (AUC:0.690, 0.614-0.750) compared to obesity-pBMI (AUC:0.541, 0.476-0.610) or obesity-FM% (AUC:0.500, 0.395-0.500)(p=0.005). Prediction of 2 or more adverse outcomes was better with MS classification (AUC: 0.781), but this was not statistically significant.

Conclusions:
MS profiling in early-pregnancy better predicts perinatal complications and offers greater clinical utility than obesity status, which poorly reflects metabolic health.

Funding: financially supported by the Instituto Nacional de Perinatología (No. 3300-11402-01-575-17).

Key-words: (up to 5):
Metabolic Syndrome, Pregnancy, Obesity, Adiposity, Perinatal Outcomes

Abstract #00004834 en

Placental adaptations in metabolically healthy obese pregnancies may improve umbilical cord DHA status by favoring DHA transfer to the fetus

Mechanisms Determining Transgenerational Effects of Health and Disease

Ferreira Carolina (1), Saraiva Marcelle (1), Belcastro Lívia (1), Reis Desirée (1), Vigor Claire (2), Pinto Gabriela (1), Barbosa Agny Julia (1), Mucci Daniela (1), Oger Camille (2), Galano Jean-Marie (2), Torres Alexandre (1), Durand Thierry (2), Burton Graham (3), Sardinha Fátima (1), El-Bacha Tatiana (1)
(1) Universidade Federal do Rio de Janeiro, (2) Université de Montpellier, (3) University of Cambridge

Background/aims:
Maternal obesity is a risk factor for adverse outcomes and is associated with a predisposition to metabolic diseases in adulthood. Adequate dosahexaenoic acid (DHA; 22:6 n-3) supply is essential for fetal growth and brain development. Altered placental lipid metabolism has been reported in obese pregnancies, compromising fetal fatty acid supply. However, we previously showed that placental lipid handling in metabolically healthy obese pregnancies was not compromised by the higher content of F4-Neuroprostanes, a product of non-enzymatic oxidation of DHA (10.3390/nu13082768). This study aimed to evaluate essential fatty acid status in umbilical cord of metabolically healthy obese pregnancies and associate it with placental lipid mediators.

Methods:
Placental fragments and umbilical cord plasma from obese (n=5) and lean (n=5) women from a cohort in Rio de Janeiro (Ethics: CAAE 34611513.0.0000.5257), were analyzed. Fatty acid profile was analyzed by gas chromatography, DHA status was assessed by DHA-to-docosahexaenoic acid (DPA; 22:5 n-6). Placental fatty acid binding protein-1 (FABP1) expression was evaluated by Western Blotting and total F4-Neuroprostanes by microLC-MS/MS.

Results:
All pregnancies were at term and neonatal parameters were within the recommended range and similar between groups. Placental and umbilical cord plasma fatty acid profiles were similar between groups. However, obese women had higher DHA status and DHA-to-alpha-linoleic acid (ALA; 18:3 n-3) ratio in the umbilical cord compared to lean women. Placental F4-NeuroP was positively correlated to umbilical cord DHA content and to DHA-to-ALA ratio; placental FABP1 was negatively associated to DHA status in umbilical cord.

Conclusions:
The results suggest that in metabolically healthy obese pregnancies, placental metabolism of n-3 fatty acids may favor DHA transfer to the fetus, thereby improving DHA status in the umbilical cord. This may have a beneficial impact on the lifelong health of the offspring.

Funding:
CNPQ; FAPERJ; CAPES

Key-words: (up to 5):
Maternal Obesity; Metabolically Healthy Obesity; Placental Fatty Acids Metabolism; DHA status in Umbilical cord

Abstract #00004835 en

Capsaicin inhibits the expression of inflammation related genes in an ex-vivo model of Wistar rat placentas

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

García Morales Abigail (1), Granados-Higa Gabriela (1), Lomas-Soria Consuelo (2), Avila Euclides (2), García-Quiroz Janice (2), Díaz Lorenza (2) (1)
UAM/INCMNSZ, (2) INCMNSZ

Background/aims:
The placenta sustains pregnancy by regulating multiple fetal and maternal endocrine and metabolic functions. Placental inflammation, seen in conditions like preeclampsia, obesity, and infections, involves increased expression of pro-inflammatory cytokines, such as interleukin (IL)-6, IL-1β and TNF-α. Conversely, the anti-inflammatory cytokine IL-10 acts as a feedback mechanism. Exacerbated inflammation can impair placental function, jeopardizing pregnancy. The placenta manages inflammation through sex-specific adaptations, safeguarding fetal survival and influencing fetal programming. Capsaicin (CPS), a bioactive compound present in Capsicum chili peppers, exhibits anti-inflammatory properties both systemically and in immune cells. However, its effects on placental inflammation and fetal sex-specific outcomes remain unexplored. Thus, this study aimed to evaluate whether CPS could mitigate TNF-α-induced inflammatory markers gene expression in cultured rat placental explants.

Methods:
At day 19 of gestation, placentas were collected and pooled according to fetal sex (n=4 Wistar rats). Placental explants (≈3 mm) were cultured under control conditions or exposed to an inflammatory environment induced by TNF-α (10 ng/mL), either with or without CPS (50 µM or 75 µM) for 24 h. Afterward, explants were homogenized for RNA extraction and gene expression was evaluated by RT-qPCR assay. Data was analyzed by ANOVA.

Results:
TNF-α upregulated the gene expression of all cytokine-coding genes tested (Tnfa, Il6, Il1b, Il10) and the inflammatory and oxidative stress mediator prostaglandin-endoperoxide synthase 2 (Ptgs2). CPS attenuated this effect, with the 75 µM concentration demonstrating a more pronounced reduction in cytokines and Ptgs2 expression. In general, the basal expression of inflammatory markers was lower in male compared to female placentas, with CPS exhibiting a stronger anti-inflammatory effect in those from males.

Conclusions:
CPS downregulated TNF-α-induced inflammatory markers expression in rat placental explants, suggesting its potential to reduce placental inflammation and highlighting the need for further CPS-related studies in inflammatory pregnancy complications.

Funding:
This work was supported by CONAHCyT grant G-1176 to C.L-S.

Key-words: (up to 5):
Placenta, inflammation, capsaicin, cytokines.

Abstract #00004839 en

The effect of prenatal exercise and diet on infant body composition and metabolic rate

Interventional strategies to prevent late-life outcomes resulting from early-life insults

May Linda (1), Stephenson Justin (1), Roenker Brittany (1), Kern Kara (1), Steen Dylan (1), Wisseman Breanna (2),
DeVente James (1), Mouro Steven (1), Rossa Lindsey (1), Ollmann Caitlyn (1)
(1) East Carolina University, (2) University of Rhode Island

Background/aims:
Maternal, and, thus, intrauterine environment is critical in establishing offspring future health or disease. Aerobic exercise and/or diet during pregnancy is well-established as effective for improving infant outcomes, it is unknown how prenatal exercise and/or diet provide the greatest benefit for offspring body composition and metabolism to decrease obesity risk. The purpose of this study is to examine the influence of maternal exercise metrics and diet during pregnancy on 1-month infant body composition and metabolism.

Methods:
Pregnant women were recruited and randomized to aerobic (AE), resistance (RE), combination (CE), or control (CON) groups. Participants completed 150 min/wk of supervised exercise and diet questionnaires. At 1-month, infant resting metabolic rate (RMR) and body composition (body fat-BF%, lean mass-LM%) were assessed. ANOVA, correlations, and regressions were performed to assess group differences, relationships, and predictors of 1-month RMR, BF%, and LM%.

Results:
Groups were similar in maternal and 1-month descriptors. Exercise groups were similar for BF%, LM%, with trends of increased RMR with RE (p=.12).
Trends for increased LM included exercise frequency (p=.13), duration (p-.13), and total sessions (p=.13, especially with RE and CE), and decreased intensity (p=.08) and dietary copper (p=.08);
Controlling for exercise group and attendance or exercise intensity and maternal fats, infant sex predicts 1-month BF% (Adj. R2=.45, p=.03). Controlling for exercise group, infant sex, and intensity, infant LM% is predicted by increased duration and decreased attendance and carbs in pregnancy (Adj.R2=.71, p=.01). Controlling for maternal pFats and lactate, infant RMR is predicted by increased maternal VitC, CE, exercise duration, and decreased exercise attendance during pregnancy (AdjR2=.93, p=.04).

Conclusions:
Maternal exercise metrics and diet alter 1-month infant BF%, LM%, and metabolism. Therefore, clinicians and policymakers must address appropriate maternal exercise prescription and diet to decrease offspring risk of obesity.

Funding:
National Institutes of Health #R01DK137945

Key-words: (up to 5):
pregnancy, exercise metrics, infant, metabolism, body composition

Abstract #00004843 en

Exploring Maternal Risk Factors, Adverse Birth Outcomes, and Early NCDs: A Network Approach to the First 1,000 Days

Big Data and Cohorts in DOHaD Research.

Alves-Costa Silas (1), Rodrigues Francisco (2), Piva Luiza (2), Leite Fábio (3), Batista Rosângela (1), Thomaz Erika (1), Alves Claudia (1), Ferraro Alexandre (2), Souza Bruno (1), Ribeiro Cecilia (1)
(1) Federal University of Maranhão, (2) University of São Paulo, (3) Duke-NUS Medical School

Background/aims:
We investigated the connections of pre-gestational and gestational maternal conditions on adverse birth outcomes and early NCDs at age two; and identified the communities within this complex network.

Methods:
We utilized data from the BRISA Prenatal Cohort, which included 1,383 mother-child dyads in São Luís, Brazil. Maternal risk factors, such as obesity, hypertension, sugary drink consumption, and socioeconomic status, were assessed during pregnancy. Data collection also involved dental examinations and self-reported health conditions. We developed a complex network to explore maternal exposures and childhood health outcomes, focusing on adverse birth outcomes and early NCDs like obesity, asthma, allergies, and caries by age two. Community detection revealed patterns of interconnectedness between maternal risks and childhood outcomes. All participants gave written consent (Ethics Committee (#l 4771/2008–30).

Results:
Sugary drinks and low income were linked to adverse birth outcomes. Ultra-processed foods, pre-gestational obesity, and diabetes during pregnancy related to cesarean delivery and macrosomia. Hypertension, mother age, and periodontitis were tied to preterm birth, which, in turn, was related to early weaning, early exposure to added sugars, and asthma at 2 years of age. Early NCDs at age two (obesity, asthma, allergies, and caries) were strongly linked to maternal consumption of ultraprocessed food and sugary drinks, maternal anemia and caries, low income, early sugar exposure at age two, cesarean birth, lack of exclusive breastfeeding, and maternal periodontitis. Three clusters emerged: Community 1 grouped metabolic risks; Community 2, social disadvantage and child caries; Community 3, behavioral and pregnancy-related risks. Gestational hypertension had the highest betweenness centrality.

Conclusions:
This study underscores the intergenerational persistence of health risks during the first 1000 days and their impact on early NCDs. Understanding how maternal metabolic, behavioral, and socio-economic risks interconnect is crucial for early interventions.

Funding:
Brazilian Ministry of Health/DCIT/CNPq; CAPES/PDPG-Amazônia Legal; CAPES/PROCAD Amazônia; Gates Foundation.

Key-words: (up to 5):
Maternal risk factors; Adverse birth outcomes; Early childhood NCDs; Complex network analysis.

Abstract #00004844 en

The First 1,000 Days: A Pioneering Book on Dentistry through the DOHaD Perspective

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Alves-Costa Silas (1), Oliveira Ana (1), Ferreira Elza (1), Haddad Ana (2), Paiva Juan (1), Baesse Deborah (1), Pinho Judith (1), Sousa Júnior Osvaldo (1), Ribeiro Cecilia (1)
(1) Federal University of Maranhão, (2) University of São Paulo

Background/aims:
The first 1,000 days are a critical window for preventing non-communicable diseases (NCDs), with dental caries, the most common NCD, affecting children early and predicting future health risks. This study aimed to describe the development and reach of an original literary work in this field: "The first thousand days of life: a DOHaD perspective to dentistry".

Methods:
This is a descriptive study of a technical product derived from a doctoral dissertation, which translated scientific findings from the Graduate Program in Dentistry at the Federal University of Maranhão into an educational literary work. The material was produced in both Portuguese and English and has been indexed in open educational repositories, including the ARES Repository. The development process involved a multidisciplinary team composed of subject-matter experts, graphic designers, instructional designers, language editors, and information technology professionals.

Results:
The publication is based on four key DOHaD-informed premises: (1) dental caries is linked to childhood asthma, obesity, and predicts future diabetes and cardiovascular disease; (2) ultra-processed foods and sugar are major risk factors for oral and systemic NCDs; (3) microbiome disruptors impact both oral and overall health; and (4) breastfeeding offers protective effects. The Portuguese edition received over 7,000 accesses across Brazil and countries including the US, UK, Germany, Ireland, Sweden, Japan, and others, prompting the release of an English version to expand its global reach and impact.

Conclusions:
This was the first book to explore the DOHaD framework within the field of Dentistry, contributing significantly to the advancement of theoretical understanding in the area. As an innovative educational resource, it supports professional training and the promotion of comprehensive health care. The publication has had a notable academic impact, underscoring the importance of interdisciplinary initiatives in advancing DOHaD-informed approaches on a global scale.

Funding:
Ministry of Health, Federal Government of Brazil.

Key-words: (up to 5):
First 1,000 days of life; Oral Health; Dentistry; Digital Book.

Abstract #00004845 en

Paternal exposure to methylphenidate induces behavioral abnormalities and altered brain gene expression in descendants.

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Nakano Ryota (1), Ikeda Riko (2), Yamazaki Yoshitaka (1), Munetomo-Aoki Sakiko (2), Morinaka Haruka (2), Abe Shohei (3), Isobe Hikaru (3), Hosonuma Masahiro (3), Kamijo Shotaro (1), Kaizaki-Mitsumoto Asuka (1), Numazawa Satoshi (1)

(1) Showa Medical University Graduate School of Pharmacy, (2) Showa Medical University School of Pharmacy, (3) Showa Medical University Graduate School of Medicine

Background/aims:

Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder that persists from childhood into adulthood. Although prescriptions for ADHD medications are increasing, the transgenerational effects of methylphenidate (MPH), a first-line treatment for ADHD, remain unclear. Recent studies suggest that paternal environmental factors prior to conception can exert lasting impacts on the health of offspring, potentially leading to transgenerational consequences. Therefore, we investigated the effects of paternal MPH exposure on behavior and gene expression in descendant using a mouse model.

Methods:

Six-week-old male ICR mice were subcutaneously administered MPH or saline for 21 consecutive days and mated with untreated female mice to produce the F1 generation. At nine weeks of age, F1 males were mated with untreated female mice to produce the F2 generation. At six weeks of age, both F1 and F2 were subjected to the spontaneous locomotor activity test and the elevated plus maze test to assess hyperactivity and anxiety-like behavior. Additionally, total RNA was extracted from the striatum of F1 and F2 mice, followed by RNA-seq and enrichment analysis. All animal care and experimental procedures were approved by the Institutional Animal Care and Use Committee of Showa Medical University (approval #23023 and # 24025).

Results:

In both the F1 and F2 generations, the total distance traveled in the spontaneous locomotor activity test was not significantly different between the MPH and control groups. In contrast, the elevated plus maze test showed a significant increase in the rate of entry into the open arms in the MPH group compared to the control group. Pathway analysis showed an enrichment of exocytosis-related genes involved in neurotransmission in both F1 and F2 generation.

Conclusions:

These findings suggest that MPH administration to male mice may alter behavior by affecting neurofunction in the next and subsequent generations.

Funding:

None

Key-words: (up to 5):

Methylphenidate, Behavior, POHaD, ADHD

Abstract #00004847 en

Triglycerides mediate the relationship between triiodothyronine and hypertensive disorders of pregnancy

Big Data and Cohorts in DOHaD Research.

Li Yanan (1), Fan Jianxia (1)
(1) International Peace Maternity and Child Health Hospital

Background/aims:
Thyroid hormones and triglycerides (TG) are associated with HDP. Triiodothyronine (T3) is the bioactive form of thyroid hormone, and the relationship between T3 in early pregnancy and HDP remains unclear. This study aimed to investigate the potential association between T3 and the incidence of HDP, while also exploring whether TG serve as a mediating factor in this relationship.

Methods:
The study included 13,915 pregnant women who underwent prenatal screening between January 2020 and December 2021. All participants gave written consent (Approval No. GKLW 2016-69). Logistic regression analyses were conducted to explore the relationship between T3, TG, and HDP. Causal mediation analysis was performed to investigate the mediating role of TG in the relationship between T3 and HDP.

Results:
We found that higher levels of free triiodothyronine (FT3), total triiodothyronine (TT3), and TG in early pregnancy were associated with an increased risk of HDP (all $P < 0.05$). Positive correlations were also observed between FT3, TT3, and TG (all $P < 0.05$). Mediation analysis revealed that TG mediated 32.5% of the total effect of TT3 on HDP through the average causal mediation effect. Subgroup analyses, which classified HDP into preeclampsia (PE) and gestational hypertension (GH), further indicated that TG acted as a mediator in the relationships between FT3, TT3, and PE, with mediation proportions of 17.7% and 28.8%, respectively. Among participants without overweight or obesity or gestational diabetes mellitus, the mediation effect remained significant.

Conclusions:
Higher levels of T3 in early pregnancy increase the risk of HDP, particularly PE, with TG playing an important mediating role in this relationship.

Funding:
This work was supported by grants from the National Key Research and Development Program of China (2018YFC1004602); the National Natural Science Foundation of China (82261128001, 81974235); Shanghai Hospital Development Center (SHDC12022119) to Jianxia Fan.

Key-words: (up to 5):
Triglycerides, Triiodothyronine, Hypertensive Disorders of Pregnancy, Mediation Analysis

Abstract #00004848 en

Free Triiodothyronine and Risk of Gestational Diabetes Mellitus: An Observational Study and Mendelian Randomization Analysis

Big Data and Cohorts in DOHaD Research.

Fan Jianxia (1), Li Yanan (1)
(1) International Peace Maternity and Child Health Hospital

Background/aims:
Free triiodothyronine (FT3) exerts a significant influence on glucose metabolism. The relationship between gestational diabetes mellitus (GDM) and FT3 during pregnancy is complex and inconsistently reported. Our study aims to explore the bidirectional association between FT3 during pregnancy and GDM, and to assess whether this association is causal.

Methods:
The observational analysis included two clinical studies. Study 1 involved 6,221 pregnant women and applied multivariate logistic regression analysis to investigate the association between FT3 in early pregnancy and the subsequent risk of GDM. Study 2 comprised 387 pregnant women and employed linear regression analysis to examine the impact of GDM on FT3 in late pregnancy. All participants gave written consent (Approval No. GKLW 2016-69). Additionally, genome-wide association study (GWAS) summary statistics of FT3 and GDM were used to perform a bidirectional two-sample Mendelian randomization (MR) analysis to test for causal associations.

Results:
In Study 1, after adjusting for potential confounding factors, increased FT3 levels in early pregnancy were associated with the subsequent risk of GDM [odds ratio (OR) 1.122; 95% confidence interval (CI) 1.004, 1.255; P = 0.043], and the restricted cubic spline analysis indicated a linear association (P for nonlinearity = 0.72). In Study 2, we didn't find association between GDM and FT3 levels in late pregnancy. MR analysis found a positive causal relationship of genetically predicted FT3 on the risk of GDM (OR 1.26; 95% CI 1.01, 1.57; P = 0.041), while in the reverse MR, there was no significant relationship of GDM on FT3. In addition, the sensitivity analysis illustrated the robustness of our MR results.

Conclusions:
FT3 levels in early pregnancy were positively associated with the risk of GDM, and MR analysis provided evidence supporting a causal relationship. Future studies are required to investigate this association in diverse ethnic populations.

Funding:
This work was supported by grants from the National Key Research and Development Program of China (2018YFC1004602); the National Natural Science Foundation of China (82261128001, 81974235); Shanghai Hospital Development Center (SHDC12022119) to Jianxia Fan.

Key-words: (up to 5):
gestational diabetes mellitus, free triiodothyronine, thyroid function, observational study, Mendelian Randomization

Abstract #00004852 en

Plasmalogens largely mediate the protective effect of breastfeeding on infections and chronic inflammation

Role of Infant and Young Child Feeding Practices on Long-Term Health

Burugupalli Satvika (1), Mansell Toby (2), wang Tingting (1), George Alexandra (1), Paul Sudip (1), Saffery Richard (2), Tang Mimi (2), McDade Thomas (3), Beyene Habtamu (1), Duong Thy (1), Vuillermin Peter (4), Ponsonby Anne-Louise (5), Burner David (2), Meikle Peter (1)
(1) Baker heart and diabetes institute, (2) Murdoch Children's Research Institute, (3) Northwestern University, (4) Deakin University, (5) Florey Institute of Neuroscience and Mental health

Background/aims:
Chronic inflammation has long-term health impacts across the life course. Breastfeeding substantially reduces inflammation risk, but key pathways, including the extent that this is due to protection against early life infection, are poorly understood. We aimed to investigate the relationships between breastfeeding, inflammation, infection burden, and to determine the extent to which metabolomic and lipidomic profiles associated with breastfeeding mediate these health outcomes.

Methods:
We utilised data from the Barwon Infant Study (BIS), a longitudinal birth cohort of 1,074 infants in Victoria, Australia. Infants with available breastfeeding (categorised as yes/no) clinical, metabolomic, and lipidomic data at 6 and/or 12 months were included (n = 793 at 6 months, n = 734 at 12 months). Inflammation, measured via glycoprotein acetyls (GlycA) at 6 and 12 months and infection burden, including parent-reported and medically attended infections, assessed through standardized 3-month questionnaires were used a outcomes.

Results:
Breastfeeding and inflammation were both associated with multiple classes of circulating plasma metabolomic biomarkers and lipids at 6 and 12 months. Breastfeeding showed a modest association with reduced infections by 12 months and a stronger association with lower inflammation at both time points, suggesting its anti-inflammatory effects extend beyond acute infection-related pathways. Metabolic pathways appeared to mediate these relationships. Notably, plasmalogens largely mediated the protective effect of breastfeeding on inflammation. Infection burden by 6 months was modestly associated with metabolomic and lipidomic profiles, with stronger associations by 12 months.

Conclusions:
Breastfeeding up to 12 months is linked to reduced infection and inflammation, with significant differences in metabolomic biomarkers and lipids mediating these benefits. These findings shed light on the pathways through which breastfeeding reduces inflammation and infection burden, identifying potential targets for optimising infant feeding.

Funding:
This work is supported by project grants from the National Health and Medical Research Council, Australia (NHMRC) (GTN1030701 and GTN1164212); LEW Carty Signature grant, The DHB Foundation.

Key-words: (up to 5):

Breastfeeding, infections, inflammation, lipid metabolism, plasmalogens

Abstract #00004853 en

Integrating spatial and single-nucleus transcriptomic data to assess the effects of intrauterine hyperglycemia on fetal pancreatic development

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Deng Yu (1), Wan Shuting (1), Yuan Zan (2), Yang Huixia (1)
(1) Department of Obstetrics and Gynecology, Peking University First Hospital, (2) College of Informatics, Huazhong Agricultural University

Background/aims:
Maternal pregestational diabetes mellitus (PGDM) can lead to adverse fetal outcomes, including lasting impacts on pancreatic development. However, the specific impacts of maternal PGDM on cellular functions and intercellular communication within the fetal pancreas remain poorly understood.

Methods:
We employ single-nucleus RNA sequencing and spatial transcriptomics (ST) to investigate cellular responses and spatial changes in the fetal pancreas (E16.5 and E18.5) under maternal PGDM conditions.

Results:
Our findings reveal significant cellular heterogeneity among acinar and beta cells, along with pronounced metabolic stress responses. More importantly, we observe decreased insulin secretion accompanied by the compensatory increase of Pdx1, Nkx6.2 and Mafa, and substantial alterations in cell-cell communication across multiple cell types. ST analysis further highlight enhanced spatial enrichment in cellular niches exposed to maternal PGDM.

Conclusions:
These findings provide valuable insights into the molecular mechanisms underlying fetal pancreatic response to maternal PGDM and offer a detailed spatiotemporal perspective on these processes.

Funding:
This work was supported by the National Key Research and Development Program of China (No. 2021YFC2700700) and the National Natural Science Foundation of China (No. 81830044).

Key-words: (up to 5):
single-nucleus RNA sequencing, spatial transcriptomics, pregestational diabetes mellitus, fetal pancreas

Abstract #00004855 en

Association Between Early-Life PUFAs and Childhood Cardiometabolic Health: The Born in Guangzhou Cohort Study

Impact of Early Life Exposures and Environmental Pollutants

He Jian-Rong (1), He Zhao-Cong (1), Gao Chang (2), Huang Yichao (2), Lu Jin-Hua (1), Kuang Ya-Shu (1), Qiu Xiu (1)
(1) Guangzhou Women and Children's Medical Center, (2) School of Public Health, Anhui Medical University, Hefei, China.

Background/aims:
Effects of in utero polyunsaturated fatty acids (PUFAs) on offspring cardiometabolic risk remain unclear. Maternal circulating PUFAs cannot fully represent fetal exposure due to the selective permeability of the placental barrier and fetal endogenous synthesis capacity. This study simultaneously quantified PUFA levels in both maternal and umbilical cord blood erythrocyte membranes to disentangle their distinct effects on childhood cardiometabolic risk.

Methods:
We included data from 188 mother-child pairs in the Born in Guangzhou Cohort Study, China. Gas chromatography-mass spectrometry (GC-MS) was used to quantify PUFA levels in maternal mid-pregnancy peripheral blood and umbilical cord blood erythrocyte membranes. Childhood cardiometabolic outcomes at age 9 included triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), total cholesterol (TC), and insulin levels. Linear regression models were employed to assess associations between maternal/cord blood PUFAs and offspring outcomes.

Results:
After adjustment for confounders, maternal mid-pregnancy α-linolenic acid (ALA) levels were positively associated with childhood TG and insulin. Eicosapentaenoic acid (EPA) correlated with higher LDL, while adrenic acid (AdA) was inversely linked to HDL. Total maternal PUFAs showed a positive association with insulin. In cord blood, total PUFAs, total n-3 PUFAs, and docosahexaenoic acid (DHA) were inversely associated with TG, whereas ALA exhibited a positive association. Cord blood EPA correlated with elevated LDL, while docosapentaenoic acid (DPA) and DHA were positively linked to HDL. DPA also showed an inverse association with insulin. Neither maternal nor cord blood PUFAs were associated with childhood TC or glucose levels.

Conclusions:
Early-life PUFAs are associated with childhood cardiometabolic health, with distinct patterns observed between maternal and cord blood PUFA profiles. These findings underscore the necessity of PUFA assessments to refine nutritional strategies for prenatal prevention of cardiovascular risks, offering novel insights into early-life interventions targeting the developmental origins of chronic diseases.

Funding:
China National Natural Science Foundation (82273642, 82173525, 82461160320), Guangdong Basic and Applied Basic Research Foundation (2022A1515220104, 2022B1515120080).

Key-words: (up to 5):
early life, PUFAs, childhood cardiometabolic health, birth cohort

Abstract #00004856 en

Inflammation marker glycoprotein acetyls and cardiovascular measures in children and adults: analysis of three population-based cohorts

Big Data and Cohorts in DOHaD Research.

Mansell Toby (1), Liu Richard (2), Nuotio Joel (3), Lange Katherine (2), Liu Mengjiao (4), Mensah Fiona (2), Ala-Korpela Mika (5), Raitakari Olli T (3), Lehtimäki Terho (6), Kähönen Mika (6), Saffery Richard (2), Wake Melissa (2), Juonala Markus (3), Lawlor Deborah A (7), Goulding Neil (7), Burgner David (2)
(1) Murdoch Children's Research Institute, (2) Murdoch Children's Research Institute, (3) University of Turku, (4) Nanchang University, (5) University of Oulu, (6) Tampere University, (7) Medical Research Council Integrative Epidemiology Unit at the University of Bristol

Background/aims:
Inflammation contributes to the development of cardiovascular disease, with evidence this occurs across the life course. We investigated the cross-sectional associations between inflammation and preclinical structural and functional cardiovascular measures in children and adults.

Methods:
We used data from the Avon Longitudinal Study of Parents and Children [ALSPAC] (n=6395 parents, n=5511 offspring at up to 3 time points), the Cardiovascular Risk in Young Finns Study [YFS] (n=2015 adults), and the Longitudinal Study of Australian Children's Child Health CheckPoint [CheckPoint] (n=1325 parents, n=1180 offspring). Confounder-adjusted linear regression models were used to estimate cross-sectional associations between inflammation markers (glycoprotein acetyls [GlycA] and high-sensitivity C-Reaction Protein [hsCRP]) and cardiovascular measures (systolic and diastolic blood pressure [BP]), pulse wave velocity [PWV], and carotid intima-media thickness [cIMT]).

Results:
Higher GlycA was cross-sectionally associated with higher systolic BP in all cohorts and at all ages (ALSPAC mean age 49-years: difference in mean systolic BP = 1.00 mmHg per 100 µmol/L increase in GlycA [95% CI 0.69, 1.31]; ALSPAC 24-years: 0.33 [0.03, 0.63]; ALSPAC 18-years: 0.72 [0.42, 1.02]; ALSPAC 8-years: 0.29 [0.09, 0.49]; YFS 38-years: 0.29 [0.02, 0.56]; CheckPoint 45-years: 1.01 [0.21, 1.81]; CheckPoint 12-years: 0.77 [0.25, 1.28]). GlycA was also associated with higher PWV in the ALSPAC cohort and CheckPoint adults and children (ALSPAC mean age 24-years: difference in mean PWV = 0.5 cm/s per 100 µmol/L increase in GlycA [95% CI 0.1, 1.0]; ALSPAC 18-years: 0.4 [95% CI 0.1, 0.7]; ALSPAC 8-years: 0.4 [95% CI 0.1, 0.7]; CheckPoint 45-years: 1.6 [0.9, 2.4]; CheckPoint 12-years: 0.5 [0.1, 0.9]). Higher hsCRP was generally associated with higher BP and higher PWV, particularly in adults.

Conclusions:
These findings suggest higher inflammation may contribute to higher blood pressure and PWV, even in childhood.

Funding:
The DHB Foundation, Sigrid Juselius Foundation, Finnish Foundation for Cardiovascular Research, Research Council of Finland, Australian National Health and Medical Research Council, UK Medical Research Council, Wellcome, British Heart Foundation.

Key-words: (up to 5):
inflammation, glycoprotein acetyls, blood pressure, pulse wave velocity, carotid intima-media thickness.

Abstract #00004857 en

Risk factors in the first 1000 days of life associated with childhood obesity: a systematic review and risk factor quality assessment

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Blaauwendraad Sophia (1), Kamphuis Arwen (1), Ruiz-Ojeda Francisco Javier (2), Brandimonte-Hernández Marco (2), Flores-Ventura Eduard (3), Abrahamse-Berkeveld Marieke (4), Collado Maria Carmen (3), van Diepen Janna (5), Iozzo Patricia (6), Knipping Karen (7), van Loo-Bouwman Carolien (8), Gil Angel (2), Gaillard Romy (1)
(1) Erasmus University Medical Center, (2) University of Granada, (3) Institute of Agrochemistry and Food Technology-National Research Council , (4) Danone Nutricia Research, (5) Reckitt Benckiser/Mead Johnson Nutrition, (6) Institute of Clinical Physiology, National Research Council , (7) Ausnutria B.V, (8) Yili Innovation Center Europe

Background/aims:
Early-life exposures might negatively affect foetal and infant development, predisposing children to obesity. This study aimed to systematically identify and evaluate risk factors for childhood obesity in preconception, pregnancy, and infancy, and assess their potential for future prediction and prevention strategies.

Methods:
This systematic review, (PROSPERO,CRD42022355152), included longitudinal studies from selected electronic databases published between inception and August 17th, 2022, identifying maternal, paternal, or infant risk factors from preconception until infancy for childhood obesity between 2 and 18 years. Screening and data extraction were conducted using standardized forms. We assessed risk factor quality on modifiability and predictive power using a piloted criteria template from
ILSI-Europe-Marker-Validation-Initiative.

Results:
We identified 172 observational and 5 intervention studies involving n=1.879.971 children from 37, predominantly high-income, countries. Average reported childhood obesity prevalence was 11·1%. Pregnancy and infancy risk factors were mostly studied. We identified 59 potential risk factors, 24 were consistently associated. Strongest risk factors were: higher maternal prepregnancy weight (n=28/31 positive associations from 31 studies), higher gestational weight gain (n=18/21), maternal smoking during pregnancy (n=23/29), higher birth weight (n=20/28), large-size-for-gestational-age-at-birth (n=17/18), no breastfeeding (n=20/31), and higher infant weight gain (n=12/12). Level of evidence was generally moderate due to unreliable exposure measurement, short follow-up/loss-to-follow up, and risk of confounding.

Conclusions:
We identified 7 risk factors, which were strongly associated with childhood obesity, and can contribute to future prediction and prevention strategies. These findings support implementation of prevention strategies targeting these risk factors from a clinical and population perspective, where possible integrated with implementation studies.

Funding:
This work was conducted by an expert group of the European branch of the International Life Sciences Institute, ILSI Europe. This publication was coordinated by the Early Nutrition and Long-term Health Task Force.

Key-words: (up to 5):

Childhood obesity, early life risk factors, preconception, pregnancy, infancy

Abstract #00004859 en

Mapping psychosocial adversity and child mental health in urban poor Indian households: A cluster analysis from the COINCIDE study

Impact of Early Life Exposures and Environmental Pollutants

Mukherjee Debarati (1), Mandal Siddhartha (2), Dixit Shweta (3), Rajendran Suganya (1), Ravi Deepa (1), Lobo Eunice (1), Babu Giridhara (4)

(1) Centre for Developmental and Lifecourse Research, Public Health Foundation of India, (2) CHARTS, Ashoka University, and Centre for Chronic Disease Control, New Delhi, (3) CHARTS, Ashoka University and Centre for Chronic Disease Control, New Delhi, (4) Department of Population Medicine, College of Medicine, QU Health, Qatar University

Background/aims:

Early-life adversities affect an estimated 64.3 million children in India, leading to poor developmental outcomes. While Bronfenbrenner's bioecological model posits that multiple interacting ecosystems shape child development, little is known about the combined impact of co-occurring psychosocial adversities on children's mental health.

Aims:

1. Identify and characterize psychosocial adversity clusters spanning maternal, child, household, andneighbourhood factors in urban poor Indian households
2. Examine associations between psychosocial adversity clusters and children's mental health duringmiddle-childhood

Methods:

Data were drawn from the COINCIDE study, a follow-up of the MAASTHI birth cohort (N=651-mother-child dyads, aged 4-8-years in 2023-24). All participants gave written informed consent (Ethics# IIPHHB/TRCIEC/214/2021). Thirteen psychosocial adversity indicators were assessed using validated tools. Child mental health was measured using the Strengths and Difficulties Questionnaire (SDQ). k-means clustering, an unsupervised machine learning method, was used to identify and characterize clusters of varying psychosocial adversity exposures. Associations of these clusters with SDQ scores were examined using linear regression models adjusted for confounders.

Results:

The mean age of children was 5.35 years (SD=1.04), with equal representation of boys and girls. We identified five distinct clusters of psychosocial adversities. Cluster-1 had the worst indicators, including high food insecurity, poor home learning environments, maternal depression, intimate partner violence, and child neglect, and had the highest child internalizing and externalizing behaviours. Cluster-2 had the most favourable psychosocial environment, and compared to Cluster-1, had significantly lower risk of both internalising (β [95%CI] = -0.54 [-0.76,-0.28]) and externalising (β [95%CI] = -0.61 [-0.86,-0.37]) symptoms.

Conclusions:

Our findings demonstrate the utility of cluster-based approaches in identifying co-occurring psychosocial risks and their differential impacts on child mental health. These methods can help tailor interventions to context-specific patterns of adversity across the life course.

Funding:

DBT/Wellcome Trust India Alliance Team Science Grant (IA/TSG/20/1/600023)

Key-words: (up to 5):
India, Child Mental Health, Global South, Early-life environments, Life course Epidemiology

Abstract #00004860 en

DNA methylation patterns in muscle tissue of adults born preterm very low birth weight: evidence from sibling study

Mechanisms Determining Transgenerational Effects of Health and Disease

Averianova Iuliia (1), Hauta-alus Helena (2), Ronkainen Justiina (1), Kuula Juho (3), Heiskala Anni (1), Sandboge Samuel (4), Kaseva Nina (5), Czamara Darina (6), Räikkönen Katri (7), Pietiläinen Kirsi (8), Kajantie Eero (9)
(1) University of Oulu, (2) University of Oulu, National Institute for Health and Welfare (THL), University of Helsinki,
(3) National Institute for Health and Welfare (THL), University of Helsinki, (4) National Institute for Health and Welfare (THL), University of Tampere, (5) National Institute for Health and Welfare (THL), (6) Max-Planck-Institute of Psychiatry, (7) University of Helsinki, (8) Helsinki University Hospital, University of Helsinki, (9) THL, University of Oulu, University of Helsinki, NTNU

Background/aims:
Shorter gestational age and lower birth weight have been associated with increased risks of various adult health conditions, yet the biological mechanisms underlying these long-term outcomes remain incompletely understood. Epigenetic modifications are a promising candidate. This study aimed to determine whether adults born preterm at VLBW exhibit distinct DNA methylation patterns in muscle tissue compared to their same-sex sibling controls.

Methods:
Epigenome-wide DNA methylation profiling was conducted on vastus lateralis muscle biopsy samples using the Illumina EPIC 850K array on 60 VLBW participants (mean age 29.4 (SD 2.5) years) and 55 sibling controls (mean age 29.1 (SD 5.1) years) from the Adults Born Preterm Sibling study. Methylation differences between preterm VLBW individuals and their same-sex sibling controls were analyzed using linear mixed-effect regression models, adjusting for age, sex, maternal smoking, batch effects, and estimated muscle cell-type composition. All participants gave written consent.

Results:
53 differentially methylated CpG sites were identified in muscle tissue (FDR-adjusted p-values <0.05). Of these, 50 sites showed hypermethylation and three sites showed hypomethylation in the VLBW group compared with controls. The largest effect size (β=0.07, FDR=0.001) was observed at cg27508002 annotated to SMAD9. The smallest FDR-adjusted p-value was found as cg11339777 (β=0.035,
FDR=2.04×10−12), annotated to the long non-coding RNA AL049828.1. Several CpG sites were mapped to genes involved in insulin signaling, glucose metabolism, and inflammatory pathways (e.g., ARHGAP22 (cg07957471, β=0.05, FDR=7.11×10−5), MAP2K3 (cg20744152, β=0.01, FDR=0.04). Gene Ontology enrichment identified “carbohydrate kinase activity” (GO:0019200, p=0.05) and “ribbon synapse” (GO:0097470, p=0.02) as significantly enriched pathways.

Conclusions:
These findings suggest that epigenetic modifications in muscle tissue may be a molecular link between early-life adversity and long-term health outcomes.

Funding:
Novo Nordisk Foundation, Academy of Finland, Sigrid Jusélius Foundation, Foundation for Pediatric Research, Finska Läkaresällskapet

Key-words: (up to 5):
Preterm Birth, Very Low Birth Weight, Epigenomics, DNA Methylation, Muscle Tissue

Abstract #00004863 en

Maternal pre-pregnancy BMI, gestational weight gain and cardiovascular stress response in adolescent offspring

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Kamphuis Arwen (1), Hirsch Alexander (1), Budde Ricardo (1), Roest Arno (2), Jaddoe Vincent (1), Gaillard Romy (1) (1) Erasmus University Medical Center, (2) Leiden University Medical Center

Background/aims:
Maternal pre-pregnancy overweight and excessive gestational weight gain (GWG) are risk factors for adverse cardiovascular health in offspring. Underlying mechanisms remain unclear, but may involve structural and functional developmental adaptions. To detect subtle cardiovascular adaptations not present at rest, exercise testing can be used. We examined the associations of maternal pre-pregnancy BMI and GWG with the cardiovascular stress response in adolescent offspring.

Methods:
Among 180 mother-adolescent-pairs from a population-based-prospective-cohort from early-pregnancy onwards, we obtained maternal pre-pregnancy BMI and GWG by physical measurements and questionnaire. At 16 years, offspring performed an isometric handgrip exercise with continuous heart rate and blood pressure (BP) monitoring and cardiovascular magnetic resonance imaging. Ethical considerations are satisfied by institutional medical-ethics-committee-approval.

Results:
Maternal pre-pregnancy overweight was associated with higher adolescent peak systolic BP (compared to maternal normal weight (Difference: 0.45-SDS, 95% confidence interval: 0.11-0.78), but not with systolic BP at rest or recovery. This association was present across the full range of maternal pre-pregnancy BMI and not explained by birth characteristics or adolescent BMI. No differences were observed in the response of heart rate or diastolic BP to exercise by maternal pre-pregnancy BMI across the full range, in clinical categories or by GWG. Higher GWG across the full range, but not maternal pre-pregnancy BMI or excessive GWG, was associated with higher left ventricular stroke volume, ejection fraction, and cardiac index during stress (all p-values<0.05). These associations were not explained by birth characteristics.

Conclusions:
Higher maternal pre-pregnancy BMI is associated with higher systolic BP at peak exercise during an isometric cardiovascular stress test in offspring aged 16 years, but not with an altered heart rate or cardiac response. Higher GWG is associated with an altered cardiac response to exercise in adolescent offspring. Our results highlight the importance of prevention of pre-pregnancy overweight to prevent cardiovascular diseases in offspring.

Funding:
NWO,ZonMw VIDI-Grant(09150172110034)

Key-words: (up to 5):

maternal pre-pregnancy BMI, gestational weight gain, adolescent, offspring, cardiovascular stress, exercise test, cardiovascular magnetic resonance measurements

Abstract #00004864 en

Lung function in adults born preterm with very low birth weight from young to mid-adulthood – A two-country birth cohort study

Big Data and Cohorts in DOHaD Research.

Jussinniemi Laura (1), Benum Silje D. (2), Aakvik Kristina A. D. (2), Kulmala Maarit K. (3), Jørgensen Anna P. M. (4), Andersson Sture (5), Hovi Petteri (3), Leppänen Heli-Kaisa (1), Evensen Kari Anne I. (2), Kajantie Eero (1)
(1) Clinical Medicine Research Unit, University of Oulu, (2) Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology, (3) Welfare epidemiology and monitoring Unit, Finnish Institute for Health and Welfare, (4) Department of Ophthalmology, St. Olavs Hospital, Trondheim University Hospital, (5) Children's Hospital, Pediatric Research Center, University of Helsinki

Background/aims:
Young adults born preterm with very low birth weight (VLBW; <1500g), especially those who had neonatal bronchopulmonary dysplasia (BPD), have reduced lung function compared with their term-born peers. We hypothesized that these impairments worsen between young and mid-adulthood.

Methods:
We studied two birth cohorts: HeSVA (Finland) and NTNU LBW Life (Norway) with harmonized protocols. Of the 137 participants with VLBW and 158 term-born controls who attended the mid-adulthood assessment in 2019-2021, lung function was assessed by spirometry in 115 participants with VLBW (20 with BPD) and 142 controls at mean age 36 years. The results were compared with young adulthood (22 years) spirometry in 198 participants with VLBW (32 with BPD) and 225 controls. Forced expiratory volume in 1 second (FEV1) and FEV1/FVC (FVC; forced vital capacity) ratio served as primary outcomes and were expressed as z-scores based on the Global Lung Function Initiative guidelines. Data were analysed by linear regression and mixed models. The study protocols were approved by the ethics committee at the Helsinki and Uusimaa Hospital district (HUS/1157) and by the Regional Committee for Medical and Health Research Ethics in Central-Norway (23879).

Results:
In mid-adulthood, BPD-VLBW participants had lower zFEV1 (mean difference: -1.49, 95%CI: -1.94, -1.04) and zFEV1/FVC (mean difference: -0.84, 95%CI: -1.23, -0.44) than controls. Corresponding differences for non-BPD-VLBW adults were -0.34 (95%CI: 0.60, -0.08) and -0.30 (95%CI: -0.53, -0.03). The differences in zFVC and zFEV1 between BPD-VLBW and term born controls increased from young to mid-adulthood.

Conclusions:
In mid-adulthood, adults born preterm with VLBW had reduced airflow compared with term-born controls. These differences were more pronounced among those with history of BPD, whose vital capacity also declined faster compared with their term-born peers.

Funding:
Academy of Finland (315690 and 355514), The Joint Research Committee between St. Olavs hospital and the Faculty of Medicine and Health Sciences, NTNU (FFU). A full list of funders is reported elsewhere (Jussinniemi L et al., 2024, Pediatr Res. doi: 10.1038/s41390-023-02896-5).

Key-words: (up to 5):
Lung function; Prematurity; Very low birth weight; Adulthood

Abstract #00004866 en

Cardiac autonomic function in adults born preterm with very low birth weight in mid-adulthood – A two-country birth cohort study

Impact of Early Life Exposures and Environmental Pollutants

Tasnim Zareen (1), Jussinniemi Laura (1), Tulppo Mikko (2), Morken Tora Sund (3), Evensen Kari Anne I. (4), Kajantie Eero (1)

(1) Clinical Medicine Research Unit, University of Oulu, Oulu, Finland, (2) Research Unit of Biomedicine and Internal Medicine, University of Oulu, Oulu, Finland, (3) Department of Neuromedicine and Movement Science, NTNU, Trondheim, Norway, (4) Department of Clinical and Molecular Medicine, NTNU, Trondheim, Norway

Background/aims:

Cardiac autonomic functioning is altered among children and young adults born with very low birth weight (VLBW<1500g), compared with their term-born peers. Whether these alterations persist to mid-adulthood remain unknown. We hypothesized that VLBW adults have reduced parasympathetic activity, and secondary, they have higher blood pressure than term-born controls which is partly mediated by lower parasympathetic activity.

Methods:

We studied cardiac autonomic function via heart rate variability (HRV) measurements in two birth cohorts: HeSVA (Finland) and NTNU LBW Life (Norway). Resting HRV was assessed in 107 VLBW and 142 controls (mean age 36 years). High frequency power (HFP) and root mean square of successive differences (rMSSD) served as priori outcomes. All submission conditions, ethical approvals, and welfare standards were met.

Results:

Compared with term-controls, VLBW participants had higher heart rate (HR) and blood pressure. In sex-stratified analyses, the mean differences (95% Confidence Intervals) between VLBW and controls in HFP among women were -43.4% (-63.9%, -11.3%) and among men -36.9% (-65.0%, 15.0%) lower. In rMSSD, corresponding differences among women were -18.2% (-35.6%, 4.1%) and among men 18.5% (-10.4%, 58.4%), in low frequency power (LFP) among women -23.7% (-46.2%, 10.5%) and among men 35.0% (-16.5%, 120.3%), and in low/high frequency ratio (LF/HF) among women 36.3% (4.1%, 76.8%) and among men -13.9% (-34.3%, 12.7%). Among VLBW women, higher blood pressure was mediated by mean HR, HFP, and LF/HF.

Conclusions:

Our results suggest altered autonomic regulatory control in adults born preterm with VLBW, especially women. This may partly underlie the higher blood pressure in VLBW adults.

Funding:

Academy of Finland (315690 and 355514), The Joint Research Committee between St. Olavs Hospital and the Faculty of Medicine and Health Sciences, NTNU (FFU). Full list of funders is reported elsewhere (Jussinniemi L et al., 2024, Pediatr Res. doi: 10.1038/s41390-023-02896-5).

Key-words: (up to 5):

Heart rate variability; Cardiac autonomic function; Preterm birth; Very low birth weight; Adulthood

Abstract #00004867 en

Gestational stress leads to sex-specifc bone health responses

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Manhães, Anna (1), Monnerat, Juliana (2), Nogueira, Anna Beatriz (2), Reis, Maria Luisa (2), Maciel, João (2), Rocha, Helena (3), Mentzinger, Juliana (3), Teixeira, Gabriel (3), Rocha, Gabrielle (2), Silva, Eduardo (4), Nóbrega, Antonio
Claudio (3), Rocha, Natália (3), Medeiros, Renata (2)
(1) Fluminense Federal University, (2) Department of Nutrition and Dietetics, Fluminense Federal University, (3) Department of Physiology and Pharmacology, Fluminense Federal University, (4) Analytical Laboratory of Restorative Biomaterials, Fluminense Federal University

Background/aims:
Prolonged exposure to gestational stress leads to negative consequences and contributes to a greater susceptibility to the onset of osteoporosis, but its impact on mothers and offspring throughout remains unknown. The aim of the study was to evaluate bone changes in mothers who suffered variable stress and bone health in their adult offspring's life.

Methods:
Wistar pregnant rats underwent a stress protocol (14th-21st day). After birth, offspring were divided into four groups (8 animals/group/sex) and monitored until 120 days: Control 90d(C90), Stress 90d(S90), Control 120d(C120) and Stress 120d(S120). Mother's blood was collected post-lactation for corticosterone and metabolic analyses. Mother and offspring femur was collected for DXA and biomechanics analysis (Ethics Committee 9518170621).

Results:
In stressed mothers, corticosterone was higher($p=0.04$), confirming the effectiveness of the stress protocol. There were no differences in serum concentration of osteoprotegerin, rank-Ligand, calcium and phosphorus in mothers. The stressed mothers had lower bone mineral density ($p=0.01$) and maximum strength ($p=0.04$). In 90d offspring there was no difference in body mass, while male S120($p=0.0011$) it was smaller. Regarding bone, male S90 had lower maximum strength ($p=0.03$). Moreover, female S120 showed lower bone mineral content (BMC,$p<0.001$) and higher distance between trochanters ($p=0.02$). In males S120, femur length ($p=0.0064$), midpoint of diaphysis ($p=0.01$) and midpoint of epicondyles ($p=0.01$), maximum force ($p=0.0002$), breaking force ($p=0.0036$) and elastic mode ($p=0.0099$) were lower.

Conclusions:
Maternal stress impaired bone health throughout offspring life, with a sex-specific response in which females suffered damage to bone composition while males had damage to bone structure and strength.

Funding:
CAPES, FAPERJ.

Key-words: (up to 5):
gestational stress, bone health, maternal health, metabolic programming

Abstract #00004868 en

The role of Pre-Pregnancy Body Mass Index and Gestational Weight Gain on Pregnancy Outcomes

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Pang Qianshu (1), Gao Di (1), Juan Juan (1), Su Rina (1), Guo Jiamei (1), Wang Chen (1), Yang Huixia (1) (1) Peking University First Hospital Obstetrics and Gynecology Department

Background/aims:
To evaluate independent and combined impacts of pre-pregnancy BMI and gestational weight gain (GWG) on pregnancy outcomes.

Methods:
In this retrospective cohort study of 33,383 singleton pregnancies, participants were stratified by pre-pregnancy BMI(underweight, normal, overweight, and obesity) and GWG relative to national recommendations(below, within, or above). Using normal-weight women having appropriate GWG as reference, we assessed risks of small for gestational age infants(SGA), large for gestational age infants(LGA), macrosomia, low birth weight(LBW), preterm birth, gestational diabetes mellitus(GDM), and hypertensive disorders during pregnancy(HDP) through multivariable logistic regression.

Results:
Compared to normal-weight women, overweight/obese women demonstrated significantly elevated risks of LGA (aOR 1.87-3.06), macrosomia (aOR 2.07-3.53), GDM (aOR 1.69-2.21), and HDP (aOR 2.36-5.37); underweight women showed increased SGA (aOR 1.91) and LBW (aOR 1.76) risks. Excessive GWG increased risks of LGA (aOR 2.23), macrosomia (aOR 2.66), and HDP (aOR 1.89), whereas insufficient GWG correlated with SGA (aOR 1.82), LBW (aOR 1.87), and preterm birth (aOR 1.52). The highest risks occurred in obese women with excessive GWG (LGA aOR 4.25；macrosomia aOR 5.29；HDP aOR 7.04) and underweight women with inadequate GWG (SGA aOR 3.22；LBW aOR 3.28). Notably, excessive GWG universally increased LGA and macrosomia risks across all BMI categories. Obese women with insufficient GWG exhibited no increased risks of SGA, LBW, or preterm birth, yet maintained elevated risks of LGA (aOR 2.37), macrosomia (aOR 2.13), GDM (aOR 2.34), and HDP (aOR 3.54). Similarly, overweight women with inadequate GWG showed no excess risks but higher risk of GDM (aOR 2.04).

Conclusions:
Both abnormal pre-pregnancy BMI and inappropriate GWG contribute to adverse pregnancy outcomes, and they exhibit combined effects. The current GWG recommendations for overweight/obesity might require downward adjustment.

Funding:
National Key Research and Development Program of China [grant number 2021YFC2700700].

Key-words: (up to 5): pre-pregnancy body mass index, gestational weight gain, pregnancy complications, fetal growth, maternal complications

Abstract #00004870 en

Placental Methionine Uptake and Gestational Stress: Implications for the effects on Long-Term Mental Health

Mechanisms Determining Transgenerational Effects of Health and Disease

Schroeder Mariana (1), Albrecht Christiane (1)
(1) University of Bern

Background/aims:
Prenatal stress (PNS) lays a biological and psychological foundation for increased vulnerability to mental health issues in the offspring, often impacting their emotional and behavioral development throughout life. Stress exerts its effects through various mechanisms, including glucocorticoids and nutrient variations. Here, we focused on placental transport of the amino acid methionine as a potential mechanism mediating the effects of stress on placental and hypothalamic methylation, and its long-term consequences on mental health.

Methods:
We employed a late-gestation environmental stress protocol in mice and analyzed a cohort of human placental samples from women who experienced low or moderate stress during pregnancy. All animal and human welfare regulations and ethical considerations were met (Ethics licenses BE23-2023 and 2016-00250, respectively). We investigated the one-carbon metabolic pathway and methylation status in the placenta and fetal serum in both humans and mice. Adult mice were subsequently subjected to a battery of behavioral tests to assess depression- and anxiety-like behaviors, and we examined the impact of PNS on the fetal and adult hypothalamus.

Results:
PNS increased the placental expression of the methionine transporter LAT1 in female mice and humans, disrupting the one-carbon metabolic pathway and inducing placental hypermethylation. In contrast, the hypothalamus of female fetuses and adult offspring was hypomethylated. Adult females also exhibited anxiety- and depression-like behaviors.

Conclusions:
Our findings suggest that PNS alters placental methionine uptake, particularly in females, leading to disruptions in the synthesis of the universal methyl donor S-adenosylmethionine (SAM) and global methylation patterns. These changes play a key role in fetal programming of sex-specific mental health vulnerabilities. Our data highlight alterations in placental one-carbon metabolism as a central mechanism by which PNS exerts its long-term negative effects on mental health.

Funding:
NCCR-TransCure (51NF40-185544), Lindenhof Foundation (17-15-F).

Key-words: (up to 5):
Gestational stress, placenta, methionine transport, methylation.

Abstract #00004871 en

Urinary Metabolomic Profiles in Early Childhood Obesity and Correlations with Cord Blood Biomarkers

Mechanisms Determining Transgenerational Effects of Health and Disease

CHEN ZILIN (1)
(1) Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Background/aims:
Childhood overweight/obesity may be programed in early life, but the mechanisms are unclear. Metabolomics, the global profiling of small molecules or metabolites, may reveal the mechanisms in developmental programming of childhood obesity/adiposity. We sought to identify early childhood overweight/obesity-related urinary metabolomic characteristics and their associations with early life /cord blood fetal growth-related molecules.

Methods:
In a nested case-control study of 43 pairs overweight/obesity and optimal weight children in the Shanghai Birth Cohort, urinary metabolomics were profiled by UPLC-MS/MS (Ultra Performance Liquid Chromatography-Tandem Mass Spectrometry), and corelated with obesity/overweight and adiposity indicators [body mass index (BMI z-score), body fat mass (BFM), and percent body fat (PBF)] at age 4 years, and cord blood biomarkers (IGF-I, IGF-II, IGFBP-I, IGFBP-II, IGFBP-III, C peptide, insulin, and proinsulin).

Results:
There were 47 differential urinary metabolites in overweight/obese vs. optimal weight children, only 5-Hydroxy-tryptophan and Tauro-alpha/beta-muricholic acid (TaMCA|TbMCA) remained statistically significant and decreased after adjusting for multiple comparisons. Adiposity indicators at 4 years were associated with 37 differential urinary metabolites. There were 10 differential urinary metabolites (Glycyleucine, Melibiose, 3-Hydroxyisovaleric acid, Picolinic acid, Acetic acid, Tartaric acid, Acetylglycine, Lysine, Ethylmethylacetic acid, TwMCA) which were associated with at least one fetal growth-related cord blood biomarkers (IGF-2, IGFBP-1, C-peptide, insulin and proinsulin).

Conclusions:
We identified 47 potentially differential urinary metabolics molecules related to overweight/obesity in early childhood, among which 5-hydroxy-tryptophan and TaMCA|TbMCA demonstrated the potential as metabolic biomarkers of early childhood overweight/obesity. We reported for the first time that certain urinary metabolomics molecules were correlated with cord blood fetal growth-related factors.

Funding:
the Ministry of Science and Technology of China (2019YFA0802501), the National Natural Science Foundation of China (82430104, 82125032 and 81930095)

Key-words: (up to 5):
Childhood obesity; Adiposity; Metabolites; Cord blood biomarkers

Abstract #00004878 en

The effects of maternal rheumatoid arthritis on mental disorders in offspring

Mechanisms Determining Transgenerational Effects of Health and Disease

Hosonuma Masahiro (1), Nakano Ryota (2), Isobe Hikaru (1), Yamazaki Yoshitaka (3), Abe Shohei (1), Kamijo Shotaro (2), Kusuyama Joji (4), Akiyama Masahiro (5), Inoue Eisuke (6), Momo Kenji (7), Oguchi Tatsunori (1)
(1) Dept. Medical Pharmacology, Showa Medical University Graduate School of Medicine, (2) Dept. Physiology, Showa Medical University Graduate School of Pharmacy, (3) Dept. Toxicology, Showa Medical University Graduate School of Pharmacy, (4) Dept. Biosignals and Inheritance, Grad. Sch. of Medical and Dental Sci., Institute of Science Tokyo, (5) Dept. Clin. Immuno-Oncology, Clin. Res. Inst. for Clin. Pharm. and Ther., Showa Medical University, (6) Showa Medical University Research Administration Center, Showa Medical University, (7) Div. Clinical Research, Dept. Hosp. Pharm., Showa Medical University Graduate School of Pharmacy

Background/aims:
In the population-based nationwide cohort study, the association of prenatal maternal rheumatoid arthritis (RA) with risk of mental disorders in offspring was reported. Furthermore, we investigated the trends in prescribed medications during RA pregnancies from the JMDC database, a large-scale Japanese administrative claims database and found that the risk of mental disorders in offspring was increased in pregnant with active RA compared to pregnant with inactive RA. The aim of this study is to address the effects of maternal RA phenotype on fetal neurodevelopment using a mouse model of RA.

Methods:
RA-like diseases were induced in female SKG/Jcl mice by mannan administration and confirmed by the development of arthritis, and mated with untreated male SKG/Jcl to produce the F1 generation. At six weeks of age, F1 was subjected to the spontaneous locomotor activity test and the elevated plus maze test to assess hyperactivity and anxiety-like behavior. Additionally, gene expression in the placenta at 13.5 days of gestation and cortex from F1 mice was assessed by single-cell RNA-seq and bulk RNA-seq, respectively. All animal care and experimental procedures were approved by the Institutional Animal Care and Use Committee of Showa Medical University (approval #325007).

Results:
The scores of hyperactivity were significantly increased and the scores of anxiety-like behavior were significantly decreased in the maternal RA group compared to the control group with the transcriptional change in the balance between excitatory and inhibitory neural activity in the cortex. In addition, scRNA-seq analysis of the placenta identified a gene X encoding a secreted protein with neuron-specific toxicity and fetal transfer in the SKG/Jcl placenta.

Conclusions:
RA phenotype during pregnancy in mice may affect the fetal neurodevelopment via placental-derived secreted proteins and cause behavioral abnormalities in offspring.

Funding:
JSPS Grant-in-Aid for Early-Career Scientists (24K19256)

36th The Grant of Nakatomi Foundation

Key-words: (up to 5):
Rheumatoid arthritis, Mental disorder, Neurodevelopment

Abstract #00004881 en

Prenatal exposure to heavy metal(loid)s mixture and childhood lung function: exploring sex-specific associations

Impact of Early Life Exposures and Environmental Pollutants

Garza Mayra J. (1), Alcala Cecilia S. (2), Tamayo-Ortiz Marcela (3), Mercado-Garcia Adriana (1), Rivera Rivera Nadya Y. (2), Gennings Chris (2), Téllez-Rojo Martha Maria (1), Wright Robert O. (2), Wright Rosalind J. (2), Lamadrid-Figueroa Héctor (1), Rosa María José (2)

(1) Instituto Nacional de Salud Pública de México, (2) Icahn School of Medicine at Mount Sinai, (3) Columbia University Mailman School of Public Health

Background/aims:

Prenatal exposure to environmental factors has been implicated in influencing lung health and disease trajectory throughout the life course. Reduced lung function serves as an early predictor not only of respiratory diseases but also for the development of cardiovascular disease, metabolic disorders, and premature mortality. However, the link between prenatal exposure to heavy metal(loid)s and childhood lung function, including sex-specific effects, has not been completely elucidated.

Methods:

We examined these associations in 438 mother-child dyads from the Programming Research in Obesity, Growth, Environment, and Social Stressors (PROGRESS) birth cohort in Mexico City. Prenatal metal levels (As, Cd, Co, Cu, Mn, Ni, Pb, Se, Zn) were measured in maternal blood collected during the 2nd and 3rd trimesters. Lung function in children was assessed once at ages 8–14 years. Mixture effects were assessed through repeated holdout weighted quantile sum (WQS) regression and hierarchical Bayesian Kernel Machine Regression (BKMR), stratified by sex to investigate sex-specific effects.

Results:

We observed inverse associations between the 2nd trimester prenatal metal mixture and lung function parameters in males. Specifically, higher exposure to metal mixture was associated with reductions in FEV1/FVC ratio (β = -0.33, 95% CI: -0.48, -0.16) and FEF25-75% z-score (β = -0.22, 95% CI: -0.39, -0.07). Pb, Ni and As were identified as primary contributors to the adverse effects on lung function and exhibited similar sex-specific patterns of association in both WQS and BKMR analyses. No associations were observed between 3rd trimester metal mixture and any lung function outcome.

Conclusions:

Earlier prenatal metal exposure may impair mid-childhood lung function with males being potentially more susceptible to these exposures. This work underscores the need to understand critical windows of exposure and sex-specific differences.

Funding:

This research was supported by grants from the National Institute of Environmental Health Sciences (R00ES027496, R01ES033245, U24ES028522, K99ES035894 R01ES014930, R01ES013744, P30ES023515 and R01ES021357) and the National Center for Advancing Translational Sciences (UL1TR004419).

Key-words: (up to 5):
prenatal; metals; pediatric lung function; mixture exposure

Abstract #00004883 en

Night-Time Eating, Multivitamin Consumption and Preterm Birth Risk

Impact of Early Life Exposures and Environmental Pollutants

Rodriguez-Cano Ameyalli M (1), Medel-Canchola Berenice (2), González-Ludlow Isabel (1), Estrada-Gutierrez Guadalupe (1), Perichart-Perera Otilia (1)
(1) Instituto Nacional de Perinatología, (2) Masters program in Clinical Nutrition, Instituto Nacional de Salud Pública

Background/aims:
Maternal nutrition in pregnancy influences birth outcomes and offspring health, with chrononutrition potentially linked to complications such as preterm birth (PTB). AIM: To evaluate if gestational chrononutrition influence PTB risk.

Methods:
Healthy pregnant women (n=215) from the OBESO cohort (INPer; 2017-2023) were studied. Diet (24hr-recall) and sleep-schedule were evaluated each trimester, obtaining average fasting duration (hours, last–first meal), minutes from waking-up to breakfast (AM-latency), and from dinner to sleep (PM-latency). Night-time eating (NtE, 9:00pm-5:59am in 3recalls) was registered. The presence of gestational complications (preeclampsia–PE–, gestational diabetes–GDM–, gestational hypertension–GH–), weight gain (GWG), multivitamin (MV) consumption (low:0-1trimesters, moderate:2trimesters, high:3trimesters) was recorded. Gestational age at resolution was computed (first-trimester ultrasound); PTB (<37weeks) was classified. Logistic regression models evaluated associations between chrononutrition aspects and PTB.

Results:
Mean fasting was 11.8±1.2hr; AM, PM latency were 104.4±76.7, 112.3±54.5min, respectively. NtE was present in 33%(n=71) of women. Gestational complications prevalence was 16.3%(n=35). Most women had a high MV-consumption (55.8%,n=120). PTB was present in 8.8%(n=19) of pregnancies. A higher frequency of PTB was observed with NtE (5.6% vs 15.5%;p=0.16) and with low MV-consumption (low:25%, moderate:5.6%, high:7.5%;p=0.011). Regression models showed that NtE (OR:5.76, 95%CI:1.70-19.42), low MV-consumption (OR:6.75, 95%CI:1.69-26.88), and PE (OR:8.31, 95%CI:1.65-41.75) were positively associated with a higher PTB risk. Other maternal variables in the model (R2=0.282,p=0.010) were not associated (age, obesity, parity, GDM, GH, GWG, kcal/day).

Conclusions:
NtE and low MV consumption during pregnancy may increase PTB risk.

Funding:
Project DGPIS (#FPIS2023-INPER-4257). OBESO cohort: Instituto Nacional de Perinatologia (No.3300-11402-01-575-17), FOSISS-CONACyT (No.2015-3-261661)

Key-words: (up to 5):
chrononutrition, prenatal supplementation, neonatal health, perinatal complications

Abstract #00004884 en

Preterm birth or low birthweight and risk of endometriosis in adolescence and early adulthood: a population-based register study in Finland

Big Data and Cohorts in DOHaD Research.

Alenius Suvi (1), Kajantie Eero (1), Pulakka Anna (2), Heikkilä Katriina (3), Gissler Mika (4), Metsälä Johanna (1)
(1) Clinical Medicine Research Unit, Oulu University Hospital and University of Oulu, (2) Research Unit of Population Health, University of Oulu, (3) Population Health Unit, Finnish Institute for Health and Welfare, (4) Department of Data and Analytics, Finnish Institute for Health and Welfare

Background/aims:
People born preterm or with low birthweight are less likely to have children than those born full-term. The association with endometriosis, a condition linked to subfertility, is less studied.

Methods:
The cohort included women liveborn in 1987-2013. Inform consent was not required. Endometriosis was defined as the first diagnosis (ICD-10 code N80) in public specialized health care before 31/12/2023. Gestational age (GA) and birthweight from the Medical Birth Register were categorized as: extremely preterm (EPT:<28 weeks), very preterm (VPT:28-31wk), moderately preterm (MPT:32-33wk), late preterm (LPT:34-36wk), early term (ET:37-38wk), full-term (FT:39-41wk, reference), and postterm (PT:>41wk). Birthweight categories were small for GA (SGA;<-2SD), large for GA (LGA;>+2SD), and appropriate for GA (AGA;>-2SD to ≤+2SD, reference). Logistic regression was used for analyses.

Results:
Among 786,479 women, 38,996 (5.0%) were preterm, 29,633 (3.8%) SGA, and 35,378 (4.5%) LGA. Up to age 37yr, 9,656 (1.2%) women had at least one endometriosis diagnosis. Preterm birth was not associated with endometriosis risk in unadjusted models (EPT: 0.65, 0.36-1.17; VPT: 1.01, 0.75-1.37; MPT: 0.84, 0.63-1.11; LPT: 1.10, 1.00-1.22), while ET birth was (1.06, 1.01-1.12). Adjustments indicated higher risk even among LPTs (aOR 1.12, 1.01-1.24). SGA and LGA had similar risks to AGA in unadjusted and adjusted models (SGA: 1.06, 0.96-1.18 and 1.07, 0.96-1.18; LGA: 1.03, 0.94-1.14 and 0.97, 0.87-1.08).

Conclusions:
Being born before 34 weeks or SGA/LGA is unassociated with endometriosis risk. However, LPT and ET birth may be associated with a slightly higher risk.

Funding:
Research Council of Finland (Grant 354936)

Key-words: (up to 5):
preterm birth, SGA, LGA, endometriosis, register study

Abstract #00004888 en

Impact of Parental Obesogenic Diets on Cardiac Health in Adult Rat Offspring

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Ponnampalam Anna P (1), Toor Khurram J (2), Annandale Marco (3), Vickers Mark H (2), Firth Elwyn C (2), Musson David (3), Albert Benjamin B (2)
(1) The University of Auckland, Pūtahi Manawa-Healthy Hearts for Aotearoa New Zealand, (2) The Liggins Institute, The University of Auckland, (3) The University of Auckland

Background/aims:
Cardiovascular disease (CVD) is the leading cause of premature death globally with significant sex-specific differences in disease etiology. While a poor maternal diet can increase offspring CVD risk, the impact of paternal diet on offspring heart health remains poorly understood. We therefore assessed the long-term effects of a parental high-fat:high-sugar obesogenic (OB) diet on cardiac outcomes in adult rat offspring (Animal Ethics: AEC26450).

Methods:
Male (pat) and female (mat) rats were fed a control (CON) or OB diet for five-weeks pre-mating. Females continued their diets throughout gestation and lactation. Four groups were established: matCON-patCON, matCON-patOB, matOB-patCON, and matOB-patOB. Following weaning, offspring were fed a standard chow diet. Echocardiography was undertaken at postnatal day 160 and heart tissues were collected and weighed.

Results:
Left ventricular mass (LVM) and posterior wall thickness (LVPW) were increased in matCON-patOB group compared to matCON-patCON, with an overall paternal diet effect on LVM and LVPW and parental diet interaction for LVPW in males. Paternal diet decreased females' normalised heart weight.
Ejection fraction (EF), fractional shortening (FS) and stroke volume (SV) were reduced in male matCON-patOB offspring compared to matCON-patCON offspring. There was an overall patOB diet effect on EF and FS in both sexes with an interaction with matOB further reducing SV in males. Cardiac output was decreased in matOB-patOB compared to matCON-patCON in females. MatOB diet reduced left ventricular end diastolic volume (EDV) in females. Parental diet interactions for EDV and LVM/EDV ratio were observed in males. There were no effects of parental diets on offspring heart rates.

Conclusions:
A patOB diet resulted in adverse sex-specific effects on cardiac outcomes in adult offspring with greater impacts in combination with matOB diet in some parameters.

Funding:
Auckland Medical Research Foundation; Pūtahi Manawa-Healthy Hearts for Aotearoa New Zealand

Key-words: (up to 5):
Parental obesity; Offspring cardiac health; Cardiac programming

Abstract #00004889 en

Associations among prenatal exposure to per-and polyfluoroalkyl substances, maternal DNA methylation, and birth size in the Atlanta African American Maternal Child Cohort

Impact of Early Life Exposures and Environmental Pollutants

Tan Youran (1), Dunlop Anne (1), Everson Todd (1), Smith Alicia (1), Eick Stephanie (1), Tang Ziyin (1), Barr Dana (1), Kannan Kurunthachalam (2), Ryan P.Barry (1), Marsit Carmen (1), Liang Donghai (1) (1) Emory University, (2) Wadsworth Center

Background/aims:
Exposures to per- and polyfluoroalkyl substances (PFAS) have been linked to reduced birth size, although underlying mechanisms remain unclear. We aimed to investigate associations of prenatal PFAS exposures with maternal DNA methylation and assess whether methylation at selected CpG sites is associated with infant birth size.

Methods:
Among 296 mother-infant dyads in Atlanta African American Maternal-Child Cohort (2016-2020), maternal blood samples collected in early pregnancy were processed to obtain serum for PFAS measurement and peripheral blood mononuclear cells for DNA methylation profiling using Illumina HumanMethylation EPIC BeadChip. Birth size was assessed using sex-specific birthweight Z-scores (BWZ, continuous) and small-for-gestational age (SGA, categorical). Robust generalized linear regression and quantile g-computation was used to estimate the effect of individual PFAS and PFAS mixture on DNA methylation, respectively. Differentially methylated regions (DMRs) analysis and gene ontology enrichment analysis were performed on PFAS-associated CpG sites. We estimated associations between methylation of significant CpG sites and DMRs with birth size.

Results:
Multiple maternal serum PFAS levels were significantly associated with higher odds of SGA, including PFOA (OR=1.92, 95%CI: 1.01, 3.75), PFNA (OR=1.37, 95%CI:1.04, 1.84), and PFAS mixture (OR=1.30, 95%CI: 1.00-1.68). After adjusting for covariates, 134 CpG sites were significantly associated with at least one PFAS levels (FDR<0.05), 2 overlapped between PFOS and PFOA, with PFOS exhibiting the greatest effect and as the main driver within PFAS mixture. Specifically, 6 CpG sites annotated to genes EVA1A, FCRL1, PRPSAP1, CTIF, ABHD12, WDYHV1, were associated with both PFAS levels and birth size . We identified 2-9 DMRs for each PFAS and PFAS mixture. The PFAS-associated genes are involved in inflammatory response, immune activity, and lipid homeostasis.

Conclusions:
Prenatal PFAS exposure could affect DNA methylation levels, suggesting potential associations with infant birth size.

Funding:
Key-words: (up to 5):
PFAS, Epigenomics, Mixtures, Birth outcomes.

Abstract #00004897 en

Impact of variable stress during pregnancy on vascular function and metabolic parameters of Wistar rat mothers

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Maciel João (1), Souza Pedro (1), Luchetti Bianca (1), Monnerat Juliana (1), Mentzinger Juliana (1), Nogueira Anna Beatriz (1), Manhães Anna Caldas (1), Reis Maria Luisa (1), Teixeira Gabriel Fernandes (1), Lima Gabriel Ferreira (1), Motta Nadia Alice Vieira da (1), Brito Fernanda Carla Ferreira de (1), Rocha Helena Naly Miguens (1), Rocha Natalia Galito (1), Nóbrega Antonio Claudio Lucas da (1), Medeiros Renata Frauches (1)
(1) Federal Fluminense University

Background/aims:
Gestational stress (GS) is a risk factor for cardiovascular disease, affecting maternal and fetal health. The aim of the study is to evaluate the impact of GS on vascular function, lipid and antioxidant profile in rats.

Methods:
Wistar pregnant rats were divided into two groups: control (C) and variable stress (VS). VS underwent an unpredictable stress protocol from the 14th to the 21st day of pregnancy. Capillary blood was collected for glucose analysis. After birth, both groups were monitored until the end of lactation and euthanized. Blood was collected for metabolic and antioxidant analysis, and thoracic aorta for vascular reactivity and protein expression analysis performed by Western Blot (eNOS, peNOSser1177 and Glutationa Peroxidase(GPx)(Ethics Committee 9518170621).

Results:
Stress protocol was confirmed by higher corticosterone values ($p=0.04$) in VS group. Regarding serum analysis, VS had a higher percentage of platelet aggregation induced by ADP($p<0.01$), and decrease in HDL($p<0.01$). Glucose was lower in VS after stress protocol ($p=0.02$). Total cholesterol, LDL, triglycerides, Castelli I and II risk index, glucose after lactation, superoxide dismutase and catalase were not significantly different. Concerning vascular reactivity, VS increased contraction response to phenylephrine($p=0.05$). For protein expression, VS expression of peNOS was lower ($p=0.007$). No significant results were obtained, neither for eNOS or GPx.

Conclusions:
Gestational stress lead to impaired vascular function, alteration of lipid profile and increase of platelet aggregation, which may be related to enhanced cardiovascular risk.

Funding:
CAPES, FAPERJ.

Key-words: (up to 5):
Variable stress, vascular reactivity, platelet aggregation, pregnancy, oxidative stress.

Abstract #00004899 en

CHRONIC CAFFEINE INTAKE AND ITS TRANSGERATIONAL EFFECTS ON REPRODUCTIVE FUNCTION IN HETEROGENEOUS FEMALE MICE

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Lopes Ferreira João Vitor (1), Carvalho Cardoso Lucas (2), de Mérici Domingues e Paula Thais (2), Campos Lobato de Almeida Fernanda (2)
(1) Laboratory of Structural Biology and Reproduction (LABER) Federal University of Minas Gerais (UFMG), (2) Laboratory of Structural Biology and Reproduction (LABER), Federal University of Minas Gerais (UFMG)

Background/aims:
Caffeine is the most widely consumed psychoactive molecule in the world, yet its transgenerational effects on female reproductive capacity remain poorly understood. This study aimed to investigate the transgenerational impacts of maternal caffeine consumption during pregnancy and lactation

Methods:
Female Swiss mice were allocated into four experimental groups (n=6/group):CC–no caffeine intake; CT–no caffeine during gestation+120 mg/kg/day during lactation; TC– 120 mg/kg/day during gestation+no caffeine during lactation; TT–20 mg/kg/day during both gestation and lactation. Caffeine supplementation, equivalent to approximately 4.2 cups (150 mL each) of coffee/day, was administered exclusively to the parental generation. The F1 generation was monitored for body growth, puberty onset, and estrous cycle assessment, then mated to generate F2, which was also evaluated for reproductive parameters. The F2 female offspring were assessed similarly, except for copulation. Ovaries from both generations were collected and processed for histomorphometrical analysis. Data were analyzed through ANOVA using the SAS software, and means were compared by the Tukey-Kramer post hoc test. Ethical approval:CEUA-UFMG

Results:
In F1, the CT and TT groups had significantly impaired body development ($P<0.05$). All caffeine-treated groups exhibited delayed vaginal opening, with TC and TT showing the most pronounced delays($P<0.05$). A reduction in all follicular categories and increased follicular atresia were observed in all caffeine-treated groups($P<0.05$), with the TT group showing the smallest litter size($P<0.05$). In F2 females, the CT group presented the largest luteal phase and the most severe folliculogenesis impairment($P<0.05$). All caffeine-treated groups showed a small proportion of preantral follicles($P<0.05$).

Conclusions:
Maternal caffeine intake during pregnancy and/or lactation induced transgenerational adverse effects on growth, development, and reproductive health. Such deleterious effects were more pronounced when caffeine was consumed during lactation. These findings reaffirm the need to avoid caffeine consumption during pregnancy and lactation.

Funding:
Conselho Nacional de Desenvolvimento Científico e Tecnológico-CNPq

Key-words: (up to 5):
Folliculogenesis-caffeine-transgenerational-ovary-offspring

Abstract #00004904 en

Gestational stress decreases insulin sensitivity, and aerobic exercise attenuates this effect in a sex-specific manner in Wistar rats

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Silva Reis Maria Luísa (1), Arruda de Souza Monnerat Juliana (1), Nogueira Anna Beatriz (1), Caldas Manhães Anna (1), Barreda Maciel João (1), Fernandes Teixeira Gabriel (2), Mentzinger Juliana (2), Rocha Luiza (2), Naly Miguens Rocha Helena (2), Claudio Lucas da Nóbrega Antonio (2), Galito Rocha Natalia (2), Souza Rocha Gabrielle (1), Frauches Medeiros Renata (1)

(1) Department of Nutrition and Dietetics, Fluminense Federal University, (2) Department of Physiology and Pharmacology, Fluminense Federal University

Background/aims:

Exposure to stress during pregnancy can impact fetal development and increase the risk of cardiovascular disease in adult offspring, while aerobic exercise is non-pharmacological intervention capable of mitigating stress-induced damage. The study aims to evaluate sex-specific responses to gestational stress on cardiac oxidative status and the role of aerobic training.

Methods:

The offspring was divided into three groups(n=8/group/sex) of Wistar rats (ethics committee 9518170621): Control(C), Stress(S), and Stress+Training(ST). The stress protocol was carried out from 14th to 21st day of pregnancy, daily, through 4 different stimuli. ST at 60 days of life underwent treadmill training for 2 months, 5 days/week. At the end of the protocol (120D), oral glucose tolerance, insulin sensitivity tests and lipid profile were conducted. Left ventricle was collected for protein expression of redox homeostasis by Western Blot (NOX2, NOX4, GPx).

Results:

The effectiveness of the stress protocol was confirmed by the increase in maternal corticosterone ($p=0.04$). Training was efficient, since animals ST reached greater speed (Male $p=0.003$; Female $p<0.001$). Concerning Insulin Sensitivity Test S females had a greater resistance ($p=0.02$) vs C and training prevented it, while the ST males presented better resistance vs S and C ($p=0.02$). Regarding oral glucose tolerance test the ST females obtained better tolerance ($p=0.03$). S Females had higher serum triglycerides ($p=<0.001$) vs C. ST males had higher serum triglycerides vs C without differences in serum cholesterol, LDL and HDL. In the left ventricle, only female ST had lower expression of NOX4 vs S ($p=0.01$).
There were no differences in other oxidant markers for both sexes.

Conclusions:

Gestational stress decreased insulin sensibility only in females and aerobic training prevented this damage, with no difference in oxidative stress proteins in cardiomyocytes.

Funding:

CAPES, FAPERJ.

Key-words: (up to 5):

metabolic programming, oxidative stress, sexual dimorphism

Abstract #00004907 en

Independent and Synergistic Effects of Maternal and Paternal Obesogenic Diets on Early Life Outcomes in Sprague-Dawley Rats

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Toor KJ (1), Vickers MH (1), Abbasi M (1), Muralidharan S (1), Ponnampalam AP (2), Musson DS (3), Albert BB (1)
(1) Liggins Institute, The University of Auckland, (2) Department of Physiology, The University of Auckland, (3) Department of Nutrition and Dietetics, The University of Auckland

Background/aims:
Independent effects of an obesogenic maternal or paternal diet on offspring outcomes are acknowledged. However, there remains limited data on the effects of combined parental obesity. We investigated the independent and synergistic effects of a parental obesogenic (OB) high-fat:high-sugar diet on offspring outcomes.

Methods:
Male (pat) and female (mat) rats were fed a control diet (CON) or OB diet for five-weeks pre-mating (Animal-EthicsAEC26450). Females continued their diets throughout gestation and lactation. Four groups were established: matCON-patCON, matCON-patOB, matOB-patCON, and matOB-patOB. Offspring outcomes included birthweights and naso-anal (NA) lengths, survival rates to weaning, weaning-weights, and retroperitoneal-fat mass. Data were analysed via two-way factorial ANOVA and survival-analysis.

Results:
Male and female birthweights were lower ($p<0.001$) in matOB-patCON and matOB-patOB groups compared to matCON-patCON and matCON-patOB groups. For males this was reflected in overall maternal effect ($p<0.001$), paternal effect ($p<0.05$), and maternal:paternal interaction ($p<0.05$), but for females this was due to maternal diet ($p<0.001$). NA-lengths in matOB-patOB male and female offspring were shorter ($p<0.001$) than other groups with overall maternal and paternal diet effects ($p<0.001$ and $p<0.05$ respectively), and a maternal:paternal diet interaction for males ($p<0.001$). Neonatal mortality was higher in the matOB-patOB group compared to the matCON-patCON group ($p<0.05$). Survival-analysis until weaning showed higher mortality in matOB-patCON offspring ($p<0.05$) and was greatest in the matOB-patOB group ($p<0.001$). Weaning weights in OB groups were increased compared to matCON-patCON group. Relative retroperitoneal-fat mass in both sexes was increased in matOB-patCON and matOB-patOB offspring compared to matCON-patCON group ($p<0.05$).

Conclusions:
We observed significant independent and synergistic effects of parental exposure to an OB diet. PatOB, combined with matOB, resulted in greater adverse impacts on birthweights and early-life survival rates compared to matOB alone.

Funding:
Auckland Medical Research Foundation.

Parental-obesity; High-fat high-sugar.

Key-words: (up to 5):

Abstract #00004914 en

Voyaging towards sustained DOHaD-Informed Policy and Practice: Lessons from a decade-long partnership between the Liggins Institute and the Cook Islands

Public Health Policies Across the Life Cycle.

Bay Jacquie (1), Tungane Cochrane Danielle (1), Barrett-Watson Celeste (2), Yaqona Delaney (2), Bates Metua (3), John Tania (3), Ngamata Karen (3), Trask Suzanne (1), Vickers Mark (1)
(1) University of Auckland, (2) Cook Islands Ministry of Education, (3) Te Marae Ora Cook Islands Ministry of Health

Background/aims:
Pacific Island Countries and Territories (PICTs) face significant health burdens. Impacts from colonization, globalization, and climate change on environmental exposures across generations are expressed in the region's obesity and NCD crises. In 2012, the New Zealand Ministry of Foreign Affairs and Trade (MFAT) identified synergies between sustainable development goals prioritised by PICTs and the Liggins Institute's DOHaD knowledge translation programmes. MFAT facilitated engagement between Pacific leaders and Liggins researchers to consider transdisciplinary collaboration. A partner-designed bid utilising DOHaD and local evidence to promote life course health was successful. This case study investigates learnings from a decade of DOHaD-informed knowledge translation in the Cook Islands.

Methods:
Case study research utilises multiple data sources to investigate complex phenomena within real-life contexts. Drawing on evidence tracking project design, outputs and impacts we examine how and why the Pacific Science for Health Literacy Project has resulted in education and science communication about transgenerational health being embedded into education and health policy and practice in the Cook Islands. Ethics: UAHPEC:#22814; CINRC:#22-21

Results:
From 2013-2024, developments from this partnership included school-based programmes (8), research studies: mother-child (1), adolescent (4), science communication (5), and professional development on transgenerational health, research methods, health promotion, science communication and statistical literacy. Successful programmes evolved gradually from locally driven needs, were co-designed, embedded into business-as-usual, and designed to be ongoing via local leadership. Long-term, influences are visible in strategies such as the national 100-year wellbeing vision (2021-2121), integration of early-life and adolescent health promotion into national NCD risk reduction strategies in health and education, and DOHaD theming of the 2025 national health conference.

Conclusions:
Factors promoting sustained DOHaD-informed policy and practice in the Cook Islands include recognition of need, co-design, trust, respect for local expertise, and embedding into business-as-usual.

Funding:
NZMFAT PF-1-280/PF-11-613; NZHRC Ref20/284

Key-words: (up to 5):
DOHaD-Knowledge-translation; Policy-&-Practice; Pacific; Education-&-Science-Communication

Abstract #00004916 en

Epigenome-wide association study implicates inflammation as the key pathway in developmental programming of cognition

Impact of Early Life Exposures and Environmental Pollutants

Mansuri Sohail Rafik (1), G V Krishnaveni (2), Sahariah Siraj (3), Sargoor Veena (2), Gandhi Mira (4), Zekveld Corlia (5), Kalyanaraman Kumaran (5), Fall H D Caroline (5), Chandak Giriraj Ratan (1)
(1) CSIR-Centre for Cellular and Molecular Biology, Hyderabad, Telangana, India, (2) Epidemiology Research Unit, CSI Holdsworth Memorial Hospital, Mysore, India, (3) DY Patil School of Public Health, Navi Mumbai, India, (4) Centre for the Study of Social Change, Mumbai, Maharashtra, India, (5) MRC Lifecourse Epidemiology Centre, University of Southampton, Southampton, UK

Background/aims:
Early-life environment is known to influence cognition, potentially via epigenetic mechanisms, including DNA methylation (DNAm). We conducted the first epigenome-wide association study (EWAS) of childhood cognition and explored the influence of early-life exposures on DNAm.

Methods:
Blood DNAm was measured using EPIC arrays in SARAS KIDS (age=5-7 years) and Mysore Parthenon Cohort (MPC) at ages 5 and 21 years. Cognition was measured by age-appropriate, culturally validated psychometric tests at 5 years in SARAS KIDS and at 9.5, 13.5, and 21 years in MPC (n=~509). General intelligence ('g') was calculated using the first principal component derived from seven cognitive tests. Discovery EWAS of cognition was conducted on 681 SARAS KIDS, and top signals were replicated in 426 independent SARAS KIDS. Stability of DNAm signatures and association were investigated in MPC at different ages. Epigenetic inflammation score (EIS), generated using six robustly reported inflammation-associated CpGs, was used as a proxy of inflammation to investigate the mechanistic aspects of the association.

Results:
EWAS identified seven differentially methylated CpGs (DMCs) mapping to inflammation-related genes, including NLRC5, SOCS3, and IFITM1 (standardized beta (sβ) range=0.19-0.23, FDR<5%), which were replicated in 426 independent SARAS KIDS. The same DMCs were also significantly associated with 'g' at all three later ages (sβ=0.13-0.28) and in a cross-sectional EWAS in 21-year-olds in MPC (sβ=0.13-0.21). Enrichment analysis identified pathways like JAK-STAT and interleukin signalling, confirming the role of inflammation, which was substantiated by the negative association of EIS with 'g' at all time points. Lower socioeconomic status, lower folate, and higher homocysteine in mothers during pregnancy were associated with higher EIS, lower child DNAm at the above loci, and lower cognition (sβ=- 0.10-0.27).

Conclusions:
This study supports the hypothesis that early-life exposures program cognition via epigenetic regulation of inflammatory pathways.

Funding:
MRC Grant No.: MR/ N006208/1 and DBT Grant No.: BT/IN/DBT-MRC/DFID/24/GRC/2015–16

Key-words: (up to 5):
Cognition, DNA methylation, Inflammation, Early-life Exposures

Abstract #00004917 en

The MULTIEPIGEN study – effects of ancestral environmental effects on offspring health and epigenetic mechanisms

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Kartiosuo Noora (1), Rovio Suvi (1), Pahkala Katja (1), Auranen Kari (1), Nevalainen Jaakko (2), Raitakari Olli (1) (1) University of Turku, (2) Tampere University

Background/aims:
The hypothesis of epigenetic inheritance in humans has gained interest in the recent decades due to the mounting evidence on this phenomenon in animal studies. Some evidence indicates that even in humans this method of non-genetic inheritance could explain the associations between paternal exposures to various stressors and aspects of offspring health, disease and mortality. However, to date, no individual study has been able to assess this hypothesis in its all aspects in humans.

Methods:
The MULTIEPIGEN study extends the well-established longitudinal Cardiovascular Risk in Young Finns Study into a three-generational cohort of n=7341 participants aged 3-92 years, enabling exploring the effects of paternal exposome on offspring health. The study was approved by local and international ethical committees and individuals/guardians signed a written informed consent. We have used a combination of 'omics methods, family models and mediation analysis to identify the key features in male sperm non-coding RNA profiles that are both affected by exposures such as environmental toxicants, tobacco smoke, adiposity and stress, and also associated with offspring cardio-metabolic outcomes. Investigating their potential mediating role provides insights on the hypothesis of epigenetic inheritance in humans.

Results:
Our analyses show that the various paternal exposures of interest measured over the life-course are associated with offspring cardiometabolic outcomes throughout the offspring childhood, youth, or adulthood. Furthermore, the epigenome-wide analyses provide insights on the role of specific carriers of epigenetic information as potential mediators between the paternal exposures and offspring health.

Conclusions:
This study is among the first to shed light on the epigenetic inheritance hypothesis in humans and suggest that paternal exposome carries effects on offspring health, potentially via epigenetic mechanisms. Future studies should explore these phenomena in prospective settings and focus on understanding the mechanistic role of the non-coding RNA molecules uncovered in our population.

Funding:
European Research Council #742927

Key-words: (up to 5):
Epigenetic inheritance; Paternal effects; Environmental toxicants; Transgenerational effects

Abstract #00004919 en

Paternal Ketogenic Diet in Mice Programs Offspring Liver Metabolism and Physical Activity

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Stolovich-Rain Miri (1), Magrill Jamie (1), Baraghithy Saja (1), Ben-Haroush Rachel (1), Ben-Cnaan Elad (1), Volinsky Evgenia (1), Ben-Zvi Danny (1), Glaser Benjamin (2), Tam Joseph (1), Dor Yuval (1) (1) HUJI, (2) Endocrinology and Metabolism Service, Hadassah University Hospital

Background/aims:
Paternal dietary exposure is postulated to program offspring metabolism via epigenetic inheritance, but few physiologically-relevant models of this effect have been developed. Very low-carbohydrate high fat diets have become increasingly popular, although the long-term consequences on progeny have not been considered. Such diets cause the generation of ketone bodies – a liver product of fatty acids, serving as an energy source during starvation. Ketones also function in signal transduction, and are modulators of chromatin. We have assessed the effect of a paternal ketogenic diet, low in carbohydrates and rich in fat, on offspring metabolism.

Methods:
Male ICR-CD1 mice consumed a ketogenic diet ad-libitum for one month - the duration of sperm formation – which caused sustained ketosis. Keto and control males were mated with females (all on control, high-carbohydrate chow), and litters were standardized at birth to 8 pups. We performed metabolic cage analysis and assessed the phenotype of the liver and pancreas of adult progeny from 4 independent cohorts fed normal chow.

Results:
Offspring of ketogenic fathers showed increased voluntary activity and energy expenditure. The livers of keto-pups had elevated lipid content, reduced glycogen content, abnormally high hepatocyte turnover and a chronic inflammatory response.

Conclusions:
Paternal ketogenic diet programs the offspring for increased voluntary activity of offspring and enhanced liver lipid metabolism. We propose that during evolution, starvation-driven ketones programmed progeny for better coping with life-threatening starvation. However modern humans consuming a ketogenic diet may predispose their offspring to unintended metabolic and inflammatory consequences.

Funding: none

Key-words: (up to 5):
paternal, ketogenic diet, fatty liver

Abstract #00004922 en

Poverty and Socio-economic Disadvantage in Women and Men and Risks of Subfertility and Miscarriage. The Generation R Next study.

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Boxem Aline (1), Mulders Annemarie (1), van Rossum Iris (1), Bekkers Eline (1), Gaillard Romy (1), Jaddoe Vincent (1) (1) Erasmus Medical Center

Background/aims:
Poverty and socio-economic disadvantage are associated with increased risks of pregnancy complications. We assessed whether poverty and markers of social disadvantage are associated with subfertility and miscarriage risks.

Methods:
This population-based prospective cohort study from preconception onwards was conducted in Rotterdam, the Netherlands among 3,604 women and men. Exposures were poverty (household income of <€3,000/month and experiencing financial difficulties), educational level and household income. Outcomes were fecundability (probability of conceiving within a month); Subfertility (time to pregnancy or duration of actively pursuing pregnancy >12 months or use of assisted reproductive technology); Miscarriage (pregnancy loss <22 weeks of gestation). Ethical considerations are satisfied by institutional medical-ethics-committee-approval.

Results:
As compared to couples without poverty, those experiencing poverty had increased odds of subfertility (32.9% versus 50.9%, OR 2.22 [95% CI, 1.60, 3.07]). Also, as compared to high educational level, low educational level among women and men was associated with increased odds of subfertility (33.3% versus 45.2%, OR 2.04 [95% CI, 1.44, 2.89]; and 30.7% versus 40.8%, OR 1.55 [95% CI, 1.17, 2.05], respectively). As compared to a household income of ≥€6,000/month, <€3,000/month was associated with increased odds of subfertility (31.2% versus 46.3%, OR 2.15 [95% CI, 1.64, 2.82]). Similar results were observed for fecundability. These associations were only partly explained by demographic and lifestyle factors. Poverty and markers of socio-economic disadvantage were not associated with miscarriage risk.

Conclusions:
In this high-income setting, poverty and social disadvantage, characterized by low educational level and household income were associated with increased risks of subfertility. Population and individual strategies to tackle poverty and social disadvantage from preconception onwards may improve fertility outcomes.

Funding:
European Research Council Consolidator Grant (2014-CoG-648916)

Key-words: (up to 5):
Preconception, poverty, socio-economic-status, fertility, miscarriage

Abstract #00004923 en

Maternal prenatal psychological distress associates with aortic intima-media thickness in infants: the FinnBrain Birth Cohort Study

Impact of Early Life Exposures and Environmental Pollutants

Rovio Suvi (1), Aatsinki Anna-Katariina (1), Snäll Martha (1), Pahkala Katja (1), Karlsson Hasse (1), Perasto Laura (1), Raitakari Olli (1), Karlsson Linnea (1)
(1) University of Turku

Background/aims:
The origins of cardiovascular health are embedded in early life and exposure to atherosclerosis risk factors in childhood associates with increased risk for cardiovascular diseases in later life. In addition to the well-established risk factors such as elevated blood pressure, adverse serum lipid profile and smoking, psychosocial stress experienced in childhood may contribute to the development of atherosclerotic cardiovascular diseases, and thicker carotid intima-media, which is a marker of early atherosclerosis in adults. Furthermore, it has been suggested that prenatal factors such as having been born small or large for gestational age, intrauterine growth restriction, preeclampsia, and maternal smoking may all be linked with greater aortic intima-media thickness in neonates. However, the evidence on the role of prenatal stress on infant vascular structure and function remains scarce. We aimed to explore in the FinnBrain Birth Cohort Study if and how maternal prenatal psychological distress – a potentially modifiable risk factor – associates with infant aortic intima-media thickness (aIMT).

Methods:
Maternal prenatal stress symptoms were measured 2-3 times during pregnancy using Edinburgh Postnatal Depression Scale (EPDS) for depressive symptoms, Symptom Checklist-90 (SCL-90) anxiety subscale for general anxiety and Pregnancy Anxiety Questionnaire-revised (PRAQ-R2) for pregnancy-specific anxiety. Vascular ultrasonography was performed for the infant at the age of 2-3 months (n=273) and aortic intima-media thickness (aIMT) was measured.

Results:
In adjusted models, mean PRAQ-R2 across pregnancy was positively associated with aIMT. In boys, mean EPDS across pregnancy was associated with a thicker aIMT.

Conclusions:
Our results indicate that pregnancy-specific anxiety associates with thicker aIMT in both sexes, whereas maternal depressive symptoms associate with thicker aIMT in boys only.

Funding:
FinnBrain Birth cohort Study (HK) has been funded by Research Council of Finland (grant numbers 253270, 134950), Jane and Aatos Erkko Foundation, as well as Signe and Ane Gyllenberg Foundation. LK was funded by the Research Council of Finland (grant number 308176 and 325292), Yrjö Jahnsson Foundation (6847, 6976), Signe and Ane Gyllenberg Foundation, Finnish State Grants for Clinical Research (P3654), Jalmari and Rauha Ahokas Foundation, and Waterloo Foundation (2110-3601). AKA was supported by Yrjö Jahnsson Foundation, Psychiatry Research Foundation, Emil Aaltonen Foundation, Brain Foundation, Instrumentarium Science Foundation, Signe and Ane Gyllenberg Foundation,

Duodecim Finnish Medical Society, Juho Vainio Foundation and the Research Council of Finland (grant number 347640). The ultrasonography and image analysis have been funded by the State Grants for Clinical Research (OR).

Key-words: (up to 5):
prenatal stress, vascular ultrasonography, intima media thickness, infants

Abstract #00004924 en

Maternal obesogenic environment and ageing influence MASLD development in offspring partially via programmed overexpression of miR-582-5p

Mechanisms Determining Transgenerational Effects of Health and Disease

Vales Mennitti Lais (1), Carminatti Pantaleão Lucas (1), Fernandez-Twinn Denise (1), Ozanne Susan E (1) (1) University of Cambridge

Background/aims:
Maternal obesity during pregnancy is linked to an increased risk of metabolic dysfunction-associated steatotic liver disease (MASLD) in the offspring. Abnormal expression of micro RNAs (miRNAs) has been implicated in MASLD development. This study aimed to 1) explore the influence of maternal obesity on offspring susceptibility to MASLD development, 2) evaluate the potential role of programmed miR-582-5p in mediating this effect and 3) investigate ageing as a contributing factor.

Methods:
A well-established mouse model of maternal diet-induced obesity was used where obese dams are fed a high-fat diet supplemented with condensed milk and control dams are fed standard laboratory chow. Male offspring were weaned onto either a control or obesogenic diet. Hepatic lipid content, miR-582-5p levels, and gene expression of fibrosis-related genes were measured in 12-week-old offspring. For ageing-related effects, the same parameters were analysed in the 12-week, 26-week, and 12-month-old offspring. Lipid accumulation was analysed in HEPG2 cells overexpressing miR-582-5p. Animal research followed the Animals Act 1986 Amendment Regulations 2012 and received ethical approval.

Results:
12-week-old offspring born to obese dams and weaned onto an obesogenic diet had increased hepatic fat accumulation, miR-582-5p levels, and gene expression of Pparg, Col1a1, Col3a1, Col5a1, and Map3k14. Focusing on programming effects and ageing, we observed similar hepatic disturbances in 12-month-old offspring born to obese dams and weaned onto a healthy diet. In vitro, miR-582-5p overexpression increased lipid accumulation, suggesting the miRNA causatively increased triglyceride accumulation.

Conclusions:
Maternal obesity leads to programmed risk of MASLD in offspring. A post-weaning obesogenic diet accelerated the programmed development of MASLD in young offspring. However, even when fed a control diet, offspring of obese dams develop MASLD with age. MiR-582-5p overexpression is a causative mechanism underlying MASLD development/progression by driving fat accumulation.

Funding:
British Heart Foundation; Medical Research Council

Key-words: (up to 5):
Maternal obesity; offspring; MASLD; miR-582-5p

Abstract #00004925 en

What makes clocks tick? Decomposing adult epigenetic clocks to probe the early origins of accelerated epigenetic ageing

Mechanisms Determining Transgenerational Effects of Health and Disease

Mulder Rosa (1), Neumann Alexander (2), Felix Janine (2), Suderman Matthew (3), Cecil Charlotte (2) (1) Erasmus MC, (2) Erasmus Medical Center, (3) Bristol University

Background/aims:
Epigenetic clocks are widely used to estimate biological age, and accelerated epigenetic ageing (i.e. epigenetic age > chronological age) associates strongly with age-related diseases and mortality. However, little is known about how DNA methylation (DNAm) sites that make up these adult epigenetic clocks behave early in life. Using data from two large longitudinal birth cohorts, we examined individual sites in adult epigenetic clocks to characterize their patterns of change over the first two decades of life, and identify prenatal influences on these patterns.

Methods:
We examined both first-generation clocks (trained on age: Horvath, Hannum, Weidner, Zhang, and Wu; N=1051 sites) and second-generation clocks (trained on mortality or age-related indicators: PhenoAge, DunedinPACE, and TelomereClock; N=820 sites). We utilized data from our EpiDelta resource (http://epidelta.mrcieu.ac.uk/) to pinpoint when specific clock sites begin to vary between individuals ($p<1e-07$), from birth to emerging adulthood (age 18y). To probe early environmental influences on these sites, we applied elastic net regressions using the prenatal exposome, including ~50 variables, using Generation R data (N=2266) as training and testing set (including cross-fold validation on the training set) and ALSPAC data (N=809) as external validation set.

Results:
We find that clock sites (i) diverge widely in their developmental trajectories, often show non-linear change over time; and (ii) are substantially more likely than non-clock sites to vary between individuals already from birth, differences that are predictive of DNAm variation at later ages. Our preliminary exposome analysis further indicates that subsets of clocks sites are related to prenatal factors such as exposure to air pollution, maternal stress, nutrition, and gestational age.

Conclusions:
These results suggests that age(ing)-related epigenetic processes might originate – and differ between individuals – already very early in development. Understanding what drives these differences may in future help us to devise better strategies to promote healthy ageing.

Funding:
Erasmus MC, Rotterdam, Erasmus University Rotterdam; the Netherlands Organization for Health Research and Development (ZonMW); the Netherlands Organization for Scientific Research (NWO); the Dutch Ministry of Health, Welfare and Sport and the Ministry of Youth and Families; the Dutch Organization for Scientific Research (NWO 2021.042, “Snellius” www.surf.nl); the UK Medical Research Council and
Wellcome (Grant ref: 217065/Z/19/Z); University of Bristol; Sample Logistics and Genotyping Facilities at Wellcome Sanger Institute and LabCorp (Laboratory Corporation of America) using support from 23andMe; the Biotechnology and Biological Sciences Research Council (BBSRC; grant numbers BBI025751/1 and BB/I025263/1) and the Medical Research

Council (MRC; grand numbers MC_UU_12013/1, MC_UU_12013/2 and MC_UU_12013/8); European Union's Horizon 2020 Research and Innovation Programme (EarlyCause, grant agreement No 848158; STAGE; STAGE has received funding from the European Union's Horizon Europe Research and Innovation Programme under grant agreement nº 101137146. UK participants in Horizon Europe Project STAGE are supported by UKRI grant numbers 10112787 (Beta Technology), 10099041 (University of Bristol) and 10109957 (Imperial College London)); European Union's HorizonEurope Research and Innovation Programme (FAMILY, grant agreement No 101057529; HappyMums, grant agreement No 101057390); the European Research Council (TEMPO; grant agreement No 101039672); LongITools (No 874739);This research was conducted while CAMC was a Hevolution/AFAR New Investigator Awardee in Aging Biology and Geroscience Research.

Key-words: (up to 5):
DNA methylation, epigenetic clocks, early origins, prenatal exposome

Abstract #00004927 en

Muscular fitness in adolescents born preterm or small for gestational age in rural Malawi

Impact of Early Life Exposures and Environmental Pollutants

Bhattacharjee Pragga (1), Kivelä Milja (1), Evensen Kari Anne (2), Ashorn Per (3), Ashorn Ulla (3), Mangani Charles (4), Kajantie Eero (1)

(1) University of Oulu, (2) Norwegian University of Science and Technology, (3) Tampere University and Tampere University Hospital, (4) Kamuzu University of Health Sciences

Background/aims:

Each year, over 13 million babies are born preterm (<37 weeks gestation) and 23 million small for gestational age (SGA, <10th percentile). Muscular strength is a key component of fitness and a well-established predictor of general health, lifespan and functional capacity. People born preterm or with low birth weight have lower handgrip strength than their peers born at term, but previous research has been focused on high-resource settings.

Methods:

Lungwena Antenatal Intervention Study (LAIS) is a pregnancy-birth cohort in rural Malawi, originally based on a randomized trial that enrolled 1320 women to assess presumptive infection treatment by azithromycin and intensified malaria prophylaxis during pregnancy. Gestational age was confirmed by ultrasound, and the children have subsequently been followed up. When the LAIS members were approaching 17 years, we saw 815 of them at an examination including measurement of handgrip strength by dynamometer; 787 had valid handgrip strength data. Of them, 91 (11.6%) were born preterm appropriate for gestational age (AGA), 12 (1.5%) preterm SGA, 126 (16.0%) term SGA; 558 (70.9%) were born term AGA and served as a comparison group.

Results:

Among the comparison group, mean handgrip strength in the dominant hand was 32.1 kg (SD 5.9) for boys and 28.0 kg (SD 4.3) for girls. In a pooled analysis adjusting for sex and age, handgrip strength was 1.3 kg lower (95% CI 0.1, 2.4) among those born preterm AGA, 3.9 kg lower (0.9, 6.8) among those born preterm SGA and 2.4 kg lower (1.4, 3.4) among those born term SGA. Results for non-dominant hand were similar.

Conclusions:

Adolescents born preterm or SGA in a rural, low-resource setting have lower handgrip strength than their peers born at term.

Funding:

Signe and Ane Gyllenberg Foundation, Foundation for Pediatric Research, Ahokas Foundation, Finska Läkaresällskapet, Sigrid Jusélius Foundation, Research Council of Finland.

Key-words: (up to 5):

premature birth, low birth weight, hand grip

Abstract #00004930 en

Unveiling Family Food Purchase Patterns: Methodology and Insights from Loyalty Card Data

Big Data and Cohorts in DOHaD Research.

Nevalainen Jaakko (1)
(1) Tampere University

Background/aims:
Access to high time-resolution data on food purchases opens new possibilities for investigating food purchase patterns in families with children. Purchase data often accumulates automatically over long periods, offering a different perspective on families' food consumption compared to self-reported data. Benefits include insights into food prices, affordability, and long-term exposure to unhealthy diets. This presentation explores the methodological and practical possibilities and challenges of using such data in nutrition research on families.

Methods:
: We obtained individual-level food purchase data from two Finnish cohorts, each with over 40,000 consenting loyalty card holders. The observation period spanned from 9/2016 to 12/2024. The retailer, which contacted participants via email, holds a 48% market share. We reclassified purchased food items in a nutritionally meaningful way and linked them to a food composition database. Monthly purchased volumes by food groups were calculated, scaled to represent weight per daily energy intake, and analyzed using longitudinal transition models, grouped by family structure.

Results:
Food purchase data must be pre-processed to ensure comparability despite differences in household structures or retailer loyalty. Selection bias in purchase data required mitigation through sample reweighting. Food baskets contain a wide variety of foods, necessitating better classification methodologies. We illustrate insights gained from the data on families' food purchase patterns, exposure accumulation, and healthy food affordability.

Conclusions:
Food purchase data is a valuable digital resource for understanding food-related behavior in families. Its strengths include large sample size, linkage to composition and life cycle assessment databases, high time resolution, and food affordability. Effective use of loyalty card data in nutrition research requires high-quality data, skilled statistical modeling, computational power, and interdisciplinary collaboration with domain experts.

Funding:
Research Council of Finland

Key-words: (up to 5):
food purchase patterns, loyalty card data, food affordability, families

Abstract #00004931 en

Predictive factors of growth among preterm infants in the neonatal period: A secondary analysis of INTER-PRACTICE-21st from urban Pakistan

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Sachwani (Rajan) Saima (1), Lassi Zohra (2), Taani Murad (3), Haase Barbara (3), Ariff Shabina (4), Johnson Teresa (3)
(1) Aga Khan University School of Nursing and Midwifery, University of Wisconsin-Milwaukee, (2) University of Adelaide, Australia, (3) University of Wisconsin-Milwaukee, USA, (4) Department of Paediatrics and Child Health, Aga Khan University

Background/aims:
Identifying postnatal growth patterns and associated factors during the neonatal period is crucial to improve both short- and long-term outcomes for preterm infants (PTIs). Despite the importance of early growth monitoring, limited research has been conducted in this area, particularly in low-and middle-income countries (LMICs) such as Pakistan. Understanding these patterns can help inform targeted interventions and health care strategies aimed at reducing neonatal morbidity and mortality. Aim: The aim of the study was to assess growth patterns and identify predictive factors for postnatal growth failure (PGF) and rapid growth in PTIs during the neonatal period in Pakistan.

Methods:
A secondary analysis of PTIs growth during the neonatal period was conducted utilizing INTERPRACTICE-21st dataset. Growth patterns were characterized as static (point prevalence) and dynamic (change over time). Descriptive statistics were used to characterize the sample, and multivariable logistic regression was employed to identify factors associated with growth patterns.

Results:
Static and dynamic PGF were observed in 65% and 83% of PTIs, respectively, while static and dynamic rapid growth were found in 7% and 11%, respectively. Higher maternal education was associated with lower odds of static PGF (AOR: 0.81, 95% CI: 0.67–0.97). With each one-day delay in the initiation of oral feeding, the odds of static PGF increased by 1.15 (95% CI: 1.01, 1.31). PTIs not exclusively fed breast milk had lower odds of dynamic PGF.(AOR: 0.19, 95% CI: 0.06, 0.60) and higher odds of dynamic rapid growth (AOR: 8.47, 95% CI: 1.91, 37.60).

Conclusions:
There is a high burden of PGF along with a small proportion of rapid growth in the neonatal period among PTIs in urban Pakistan. Maternal education level and infant nutrition practices significantly influence growth patterns among PTIs.

Funding:
Institute for Global Health and Development at Aga Khan University, Hospital for Sick Children (SickKids), and the University of Oxford, with funding from the Bill and Melinda Gates Foundation.

Key-words: (up to 5):
Infant Nutrition, Preterm Infant, Nenoate, Postnatal Growth, Growth Failure

Abstract #00004942 en

The SPPIN Study: Cohort Profile on Social Location, Gut Microbiota, Maternal Mental Health, and Infant Development

Big Data and Cohorts in DOHaD Research.

Wowdzia Jenna (1), Serrano Lomelin Jesus (2), Van Lieshout Ryan (3), Sycuro Laura (4), Kozyrskyj Anita (5), Jain Venu (6), Krzeczkowski John (7), Pei Jacqueline (6), Walter Jens (8), Ospina Maria (2)
(1) University of Alberta / Women and Children's Health Research Institute , (2) Queens University, (3) McMaster University , (4) University of Calgary, (5) Universtiy of Alberta, (6) University of Alberta, (7) Brock University, (8) University College Cork

Background/aims:
Social location is shaped by the intersection of socioeconomic status, culture, and environment. It affects maternal mental health and child development, yet its biological mechanisms remain unclear. Gut microbiota is a potential pathway linking social conditions to health. The Society, Pregnancy, Postpartum and Infant Neurodevelopment (SPPIN) study examines how social factors influence maternal and infant gut microbiota and whether microbiota mediates effects on maternal mental health and child neurodevelopment. Here, we present the cohort design and preliminary participant profile.

Methods:
SPPIN aims to enroll 600 pregnant individuals in their second trimester using clinical, social media, community, and geographic information system-based recruitment. Data on maternal social characteristics, gut microbiota, mental health, and related factors (e.g., nutrition, medications, delivery mode, breastfeeding, bonding) are collected using validated self-report measures. Child gut microbiota and neurodevelopment are assessed up to 36 months. Assessment methods include self-reports, fecal samples, Bayley Scales, and the Coding Interactive Behaviors assessment.

Results:
Recruitment began in November 2024. A preliminary analysis of 57 participants (mean ± SD: 32.9±3.8 years old) showed a mean gestational age of 18.2±6.1 weeks. Most were pregnant with their first (n=26) or second child (n=26). Mean pre-pregnancy BMI was 26±3.5 kg/m2. Participants learned of their pregnancy at 4±1.2 weeks, and 86% reported it as planned. Most have post-secondary education (n=54), were married or in common-law relationships (n=56), and were born within Canada (n=42). Racial backgrounds primarily identified as White (n=42) with representation from other groups. Household income ranged widely, with most households reporting income above $100,000 (n=48).

Conclusions:
SPPIN recruitment is ongoing and future analyses will expand on these findings. Understanding how social environments shape maternal and child health via gut microbiota may inform predictive tools and targeted interventions to support at-risk groups.

Funding:
Canadian Institute for Health Research (#487536), Canada Research Chairs Program (CRC-2023-00153).

Key-words: (up to 5):
pregnancy, microbiome, neurodevelopment, postpartum

Abstract #00004943 en

Moment-to-Moment Associations Between Breast Milk Glucocorticoids and Infant Crying and Sleep.

Role of Infant and Young Child Feeding Practices on Long-Term Health

Bruinhof Nina (1), Beijers Roseriet (2), de Weerth Carolina (2)
(1) Radboudumc , (2)

Background/aims:
Breast milk composition has been found to fluctuate in relation to maternal and infant factors. These changes in composition may affect infant development, cortisol in mother milk has been associated with infant negative affect. However, evidence supporting the role of breast milk glucocorticoids (i.e., cortisol and cortisone) on infant behavior is inconsistent, potentially due to methodological heterogeneity and daily fluctuations in both milk cortisol and infant behavior. Furthermore, infant behavior might also affect breast milk glucocorticoids, however, this has not yet been studied. Therefore, the current preregistered study investigated bidirectional associations between diurnal breast milk glucocorticoids and infant crying and sleep. We hypothesize that 1) higher milk glucocorticoid concentrations will be related to more infant crying and less infant sleep, and 2) more infant crying and less infant sleep will be related to higher milk glucocorticoid concentrations.

Methods:
At 6 weeks postpartum, healthy mothers (N=109) collected three breast milk samples: in the morning, afternoon, and evening. During this same day, mothers kept a logbook on infant crying and sleep. We calculated the duration of crying and sleeping in three time intervals: 1) the whole interval between each breast milk sample, 2) the 1.5 hours after each breast milk sample, and 3) the 1.5 hours before each breast milk sample. Next, we performed multilevel models assess the associations between breast milk glucocorticoids and infant crying and sleep and vice versa.

Results:
Against our hypotheses, we found that higher milk cortisone was related to more infant sleep in the 1.5 hours after feeding. Moreover, more infant sleep was related to higher milk cortisol levels post-feeding.

Conclusions:
This study is the first to assess moment-to-moment associations between breast milk glucocorticoids and infant behavior and finds unexpected positive associations between milk cortisone and infant sleep.

Funding:
Netherlands Organization for Scientific Research, Vici Grant to Carolina de Weerth (016.Vici.185.038).

Key-words: (up to 5):
breast milk, cortisol, infant crying, infant sleep

Abstract #00004944 en

Infant colic and behavioral problems from childhood to adolescence – moderation by maternal childhood trauma and attachment style.

Mechanisms Determining Transgenerational Effects of Health and Disease

Bruinhof Nina (1), Latini Asia (1), de Weerth Carolina (1)
(1) Radboudumc

Background/aims:
: Approximately 25% of infants are affected by colic, defined as excessive, unsoothable crying for three or more hours per day within the first 12 weeks postpartum. While colic is a major stressor for parents and has been linked to early behavioral difficulties, its long-term association with behavioral problems from childhood to adolescence remains unexplored. Additionally, some parents may be particularly vulnerable to the stress of caring for a colicky infant, yet the role of maternal childhood trauma and insecure attachment in moderating this association between infant colic and later behavioral problems is unknown. The current study will create trajectories of children's behavioral problems across development from ages 2.5 to 16. After, we will examine whether infant colic predicts these behavioral problems trajectories, and assess whether maternal adverse childhood experiences (ACEs) and attachment insecurity moderate these associations.

Methods:
We use data from the longitudinal BIBO cohort, which includes maternally reported child behavior across eight assessment waves. Infant colic was assessed at six weeks postpartum using a four-day maternal diary. Latent class growth analysis (LCGA) will model behavioral problem trajectories, with additional predictors incorporated subsequently.

Results:
Analyses are ongoing, and findings will be presented at the conference. Importantly, previous results from the BIBO study have demonstrated the long-term role of infant colic on adolescent sleep problems (Rheinheimer & de Weerth, 2025) and steeper diurnal cortisol slopes (Brett et al., 2024).

Conclusions:
This study will provide crucial insights into the possible lasting impact of infant colic and help identify families most vulnerable to its effects.

Funding:
Netherlands Organization for Scientific Research, Grants to C. de Weerth 016.Vici.185.038 and Vidi 452-04-320.

Key-words: (up to 5):
infant crying, colic, behavioral problems, ACEs, attachment

Abstract #00004946 en

Distinct sphingomyelin species in obese and gestational diabetes mellitus pregnancies

Mechanisms Determining Transgenerational Effects of Health and Disease

Pinto Gabriela Dias Alves (1), Souza Hygor M R de (1), Ferreira Carolina dos Santos (1), Reis Desiree Lopes (1), Soliz Gabriela Raquel Amaral (1), Guimarães Maria Fernanda Costa (1), Goes Vanessa de Araújo (1), Koulman Albert (2),
Torres Alexandre Guedes (1), El Bacha Tatiana (1)
(1) UFRJ, (2) Cambridge University

Background/aims:
Gestational diabetes mellitus (GDM) and pre-pregnancy obesity are associated with adverse outcomes. Although obesity is a major risk factor for GDM,lipid metabolism, particularly sphingolipids, differs between obese and GDM pregnancies.The investigation of the mechanisms involved in alterations in sphingolipid metabolism in obesity and GDM may offer insights into intergenerational cycles of detrimental effects on metabolic health.This study aimed to characterize sphingomyelin species in maternal and cord blood, and placental tissue of obese pregnant women with and without GDM.

Methods:
Women with pre-gestational overweight/obesity (OB) and overweight/obesity+GDM (OB/GDM) were enrolled. Maternal plasma from the 3rd trimester (n=22 (OB); n=13 (OB/GDM)), placental samples (n=14 (OB); n=10 (OB/GDM)) and umbilical cord plasma (n=10 (OB); n=8 (OB/GDM)) from term pregnancies were collected from prospective cohorts in Rio de Janeiro (Ethics:
34611513.0.0000.5257;66949217.0.0000.5275).Sphingomyelin (SM) profile was evaluated by high-resolution mass spectrometry. Data was processed with Skyline software in a targeted analysis.

Results:
A total of 28 SM were found in all samples. SM 34:1 was the most abundant in all compartments, followed by SM 42:2, 40:1 and 42:1. Despite similar contents, correlation analyses between compartments showed significant differences. In the OB/GDM group, cord blood SM 34:1 positively correlated to placental SM 34:1 (r=0.833; p=0.015). Cord blood SM 40:2 negatively correlated to maternal SM 40:2 (r= -0.857; p=0.017). In the OB group, these correlations were not significant.Importantly, SM 40:2 had a receiver operating characteristic area under the curve of 0.743 (p=0.024),indicating moderate discriminatory power in distinguishing obese and GDM pregnancies.

Conclusions:
SM 34:1 contains palmitic acid, with pro-inflammatory properties, and long-chain fatty acid SM (>40 carbons) present regulatory properties in the placenta, suggesting a role of these SM species in the pathophysiology of GDM,possibly affecting the life-long health of the offspring.

Funding:
FAPERJ; CNPq; CAPES

Key-words: (up to 5):
Metabolic health; Lipids metabolism; Sphingolipds; Gestational lipid metabolism

Abstract #00004947 en

Patterns of Adverse Neonatal Outcomes in Black Brazilian Women Using K-Means and Apriori Algorithms

Big Data and Cohorts in DOHaD Research.

Cristine Silva Alves Yasmin (1), Morsoleto Ricardo (2), Mara Ferreira Miranda Simone (3), Helen Gonçalves Martins Mariana (1), Paula Mendes Marques de Lima Franco Anna (1), Helena Pereira Flávia (2), Turcatto Gimenes Faria Heloisa (2), Scotini Freitas Patrícia (1)
(1) Universidade Federal de Alfenas (UNIFAL-MG), (2) Instituto Federal de Educação, Ciência e Tecnologia do Sul de Minas - Campus Passos, (3) Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) - Bolsista nível A

Background/aims:
Disparities in the quality of prenatal and delivery care among Black women in Brazil have been associated with adverse neonatal outcomes, including prematurity, low birth weight, low Apgar scores, and congenital anomalies. This study aimed to identify maternal characteristics and care aspects associated with unfavorable neonatal outcomes in Black Brazilian women using association rule mining.

Methods:
An exploratory approach was applied to the SINASC 2023 data. Following data preprocessing to remove missing values and outliers, the K-Means algorithm was applied to cluster records based on sociodemographic and clinical variables, including maternal age, race, education, marital status, occupation, prenatal visits, birth weight, Apgar scores, and congenital anomalies. Thereafter, the Apriori algorithm was utilized to identify significant association rules.

Results:
The analysis revealed seven distinct clusters, with six predominantly composed of Black women. Cluster C1, which included a higher proportion of White women, exhibited superior neonatal outcomes characterized by higher education, stable marital status, optimal Apgar scores, and absence of anomalies. In contrast, Cluster C2 had the lowest mean birth weight (2,670 g) and consisted mainly of Black women who were single and had lower education attainment. Notably, Cluster C5, despite demonstrating adequate Apgar scores and birth weights, showed a higher occurrence of congenital anomalies. The association rule analysis further indicated that a minimum of seven prenatal consultations was significantly linked to improved neonatal outcomes, emphasizing the critical interaction between race, education, and clinical indicators.

Conclusions:
These findings suggest the persistent racial disparities in maternal and neonatal care in Brazil, underscoring the urgent need for targeted public health policies and clinical decision-support tools to address the needs of Black women.

Funding:
CNPq and the Department of Science and Technology, Ministry of Health (DECIT/SECTICS/MS).

Key-words: (up to 5):
Neonatal outcomes; Prenatal care; Racial disparities; Data mining; K-means;

Abstract #00004948 en

Prenatal exposure to acrylamide, offspring's fetal size and size at birth: A Biomarker-based Cohort Study from Denmark

Impact of Early Life Exposures and Environmental Pollutants

Chandia-Poblete Damian (1), Tuffier Stéphane (1), Vryonidis Efstathios (2), Halldorsson Thorhallur Ingi (3), Bjerregaard Anne Ahrendt (4), Rytter Dorte (5), Bech Bodil Hammer (5), Henriksen Tine Brink (6), Törnqvist Margareta (2), Olsen Sjurdur Frodi (4), Pedersen Marie (1)
(1) University of Copenhagen, (2) University of Stockholm, (3) University of Iceland, (4) Statens Serum Institut, (5) Aarhus University, (6) Aarhus University Hospital

Background/aims:
Acrylamide (AA) forms in a range of commonly consumed carbohydrate-rich foods during high-temperature cooking. Maternal exposure to AA from diet and smoking during pregnancy have been associated with reduced neonatal size at birth, but the possible impact on early fetal growth has not yet been studied. We aimed to assess the associations between prenatal exposure to AA, fetal size and size at birth.

Methods:
Exposure to AA was quantified through hemoglobin adducts from AA (HbAA) measured with a high-throughput method in blood collected in gestational week 30 from women giving birth to liveborn singletons in 1988-89, Aarhus, Denmark (N=996). Blood and maternal characteristics, clinical records of intrauterine growth restriction (IUGR), ultrasound scans of biparietal diameter (BPD) at the 16th gestational week, small-for-gestational-age (SGA), birth weight (BW), birth head circumference (BHC) and birth length (BL) of the offspring were also obtained from the Danish Fetal Origins 1988-89 cohort.

Results:
AA was associated with a small non-significant reduction in BPD. Compared to the lowest quartile, the highest quartile of HbAA were associated with increased risk for IUGR (OR=4.1; 1.2,16.0) and for SGA (OR=4.0; 1.4,13.2) and a reduction in BW of -292g (-423,-161). Each 10-pmol/g Hb increase in HbAA was associated with reduced size at birth: -11g (-18.3,-4.5) for BW, -0.05 cm (-0.09,-0.01) for BHC, and –0.03 cm (-0.07,-0.01) for BL. The magnitude of most of these associations attenuated in non-smokers (N=366) and enlarged in smokers (N=269).

Conclusions:
These findings add to the evidence that higher levels of prenatal exposure to AA is associated with reduced offspring's size at birth and calls for more research on exposure to AA early in prenatal development and growth.

Funding:
This study has been prepared as part of the CHIPS project funded by the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 758151)

Key-words: (up to 5):
Biomarkers of exposure, Birth outcomes, Pregnancy outcomes, Epidemiology, DOHaD

Abstract #00004952 en

Developing a 3D model of the bone marrow niche to investigate the influence of folate on childhood leukaemia-initiating events

Impact of Early Life Exposures and Environmental Pollutants

Saville Jessica (1), Padget Kay (2), Pal Deepali (3), Porter Kate (1), Russell Lisa (4)
(1) Northumbria University, (2) St George's University, (3) University of Bristol, (4) Newcastle University

Background/aims:
Acute lymphoblastic leukaemia (ALL) is the most common cancer in children. Although aetiology is unclear, various genetic aberrations, such as chromosomal translocations, are considered initiating events in ALL development and have been retrospectively detected at birth, suggesting they occur in utero. Further aberrations, such as epigenetic modifications, are also likely required for disease progression. Epidemiological evidence suggests maternal folate status influences risk of childhood leukaemia. Folate is known to influence DNA damage, repair and methylation status. Current guidelines recommend pregnant women consume synthetic folic acid (FA) supplements during the first trimester, however, biologically active folate, 5-methytetrahydrofolate (5mTHF), is becoming more popular in pregnancy targeted supplements. We aim to investigate the influence of FA and 5mTHF on leukaemia-initiators using organoid models to replicate the bone marrow niche.

Methods:
Mesenchymal stem cells (MSCs) were used to create 2D and 3D organoids supporting growth of GM12878 B cells in media containing physiologically relevant concentrations of FA or 5mTHF. Cell growth was evaluated through trypan blue exclusion. Intracellular and media folate levels were measured using LC-MS. Reverse-transcription PCR is used to monitor cell markers and identify leukaemia-initiating events.

Results:
When grown in co-culture with MSCs, B cell growth is increased compared to growing alone. A further increase in B cell growth was observed when grown in the presence of 3D spheroids compared to 2D monolayers of MSCs. When grown in folate deficient conditions a reduction in B cell growth compared to standard media is observed for both FA and 5mTHF supplementation over 9 days. A reduction in intracellular folate was observed as early as 2 days following folate depletion.

Conclusions:
We have optimised a 3D model of folate status in B cells, allowing us to investigate the induction of leukaemia-initiators. Such knowledge may be useful to influence public health policy for folate guidance during pregnancy.

Funding:
World Cancer Research Fund UK, as part of the World Cancer Research Fund International grant programme #IIG_FULL_2022_007

Key-words: (up to 5):
Childhood Leukaemia, Maternal Folate Status, Organoids

Abstract #00004957 en

The early life gut microbiome developmental trajectory as predictor for cognitive and behavioral development in 2-year-olds

Impact of Early Life Exposures and Environmental Pollutants

Galjaard Claire (1), Bastiaanssen Thomaz (2), de Weerth Carolina (1)
(1) Radboud University Medical Center, Donders Institute for Brain, Cognition and Behaviour, (2) Amsterdam University Medical Center, Department of Psychiatry

Background/aims:
Early life, including the first two postnatal years, is a critical period for child physical and mental development. During this time, the child's gut microbiome follows a parallel interdependent developmental trajectory with the brain. The gut microbiome has been associated with cognitive, behavioral, and sleeping problems at single time points within this critical period. This preregistered study (osf.io/vg3y6) aims to determine whether both developmental trajectories and single assessments of the early gut microbiome might be associated with cognitive, behavioral, and sleep problems at 2-year-olds.

Methods:
Fecal samples were collected at 2, 6, 12, 32 weeks, and 2 years of age as part of the ongoing, prospective, longitudinal SMILEY- study (Lustermans et al., 2024; Eckermann et al., 2025) and analyzed using shotgun metagenomic sequencing to assess gut microbial taxonomy (species), ecological alpha and beta diversity as well as neuroactive potential (gut-brain-modules). The outcomes at 2 years of age consisted of maternal questionnaires on child cognitive (BRIEF-P), behavioral (CBCL1.5-5) and sleeping (CSHQ) problems. We will use a Bayesian framework to compare trajectorial analysis to single time point analysis.

Results:
Data analysis is ongoing and expected to be completed by the end of May; therefore, we provide our expectations for the results. These are that altered early gut microbiome trajectories will be associated with worse cognitive, behavioral and sleeping problems at the age of 2 years. We also expect these associations with trajectories to be more informative than those of single assessment points.

Conclusions:
Although the results are pending, these findings will highlight if specific gut microbiome trajectories, and potentially also specific time points, may potentially function as predictors for worse outcomes in 2-year-olds. Determining and modulating these trajectories could be informative for future development of clinical interventions and early childhood healthcare strategies.

Funding:
NWO (016.Vici.185.038-to de Weerth)

Key-words: (up to 5):
microbiota, trajectories, cognition, behavior, sleep

Abstract #00004959 en

Understanding the challenges and barriers to retention in longitudinal maternal-child studies: what we can learn from Children of UPBEAT

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Kaur Simrat (1), Burden Samuel (1), Taylor Paul (1)
(1) Department of Women and Children's Health, King's College London, UK

Background/aims:
Retention in maternal-child cohort studies is fundamental in maintaining study power and population representativeness, yet it is a difficulty faced by many research groups. Understanding participant experiences and constraints is essential to designing accessible research protocols. We aimed to explore the common barriers and future suggestions to improve engagement and retention among mothers in Children of UPBEAT – a 10-year follow-up of children from the UK Pregnancies Better Eating and Activity Trial (UPBEAT).

Methods:
A mixed methods design, combining qualitative telephone interviews with a structured online survey (Qualtrics) was completed in n=74 mothers. Mothers who had missed appointments or declined follow-up were contacted by phone and asked to share reasons for non-attendance. An open-ended survey invited mothers to reflect on personal challenges and propose improvements to study design. (Ethics Committee #23/LO/0410).

Results:
As of 18th April 2025, n=238/1,555 (15.3%) UPBEAT women consented in theory to participate in Children of UPBEAT, yet only n=160 (10.3%) have completed study visits. Key themes included institutional barriers (e.g. fear that their child's school absence would be recorded as unauthorised), practical constraints (e.g. lack of weekend/evening appointments, childcare responsibilities, or inability to take time off from work), and perceived inadequacy of incentives. Many were willing to participate but identifying a suitable time was a common barrier. Suggestions included offering flexible scheduling, increasing financial reimbursement, and issuing school or work-related attendance letters to legitimise participation.

Conclusions:
This study highlights the importance of patient and public involvement and engagement (PPIE) in the design of longitudinal cohort studies. Mothers face a complex interplay of social, institutional, and logistical barriers that limit their ability to attend visits. Addressing these barriers is vital for improving retention and ensuring equitable participation in longitudinal research.

Funding:
British Heart Foundation (SP/F/21/150013).

Key-words: (up to 5):
Retention, qualitative research, cohort

Abstract #00004963 en

Leptin and Adiponectin Levels in Preterm Infants and Their Relationship with Birth Weight for Gestational Age

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Luna Leonardo (1), Vieira Erika (1), Rosa Victor Hugo (1), Suano-Souza Fabiola (1), Strufaldi Maria Wany (1) (1) School of Medicine / Federal University of Sao Paulo

Background/aims:
Prematurity and low birth weight are associated with an increased risk of chronic diseases in adulthood, such as obesity. These children tend to have a high amount of body fat. Leptin and adiponectin, which are associated with worse and better cardiometabolic outcomes, respectively, are adipokines that may serve as early markers of excess adipose tissue in this population. The aim of this study was to measure both adipokines in a group of preterm infants and compare them with a group of full-term infants.

Methods:
A cross-sectional, multicenter study was conducted with preterm infants weighing >1000g (n=27) from two University Hospitals and full-term infants weighing >2500g (n=51) from Primary Healthcare Units in the metropolitan region of São Paulo, Brazil. All participants were assessed at a corrected age between 9 and 24 months, when anthropometric measurements and serum collection of leptin and adiponectin were performed. The study was approved by the Ethics Committee of the institution.

Results:
The preterm group consisted primarily of male individuals (63%) and was assessed after the first year of life (15.2 ± 6.7mo), showing significant differences ($p < 0.05$) in birth weight and Z-scores, during the assessment, in body mass index, stature/age and head circumference. When classified according to birth weight for gestational age, leptin levels were higher (2,03 vs 0,65 vs 0,55; p=0,069), while adiponectin levels were lower (18,73 vs 62,05 vs 64,27; p<0,05) in the Small for Gestational Age (SGA) group compared to the Appropriate for Gestational Age (AGA) and Large for Gestational Age (LGA) groups, regardless of gestational age.

Conclusions:
Therefore, gestational age alone did not result in an altered adipokine profile in the studied sample. SGA infants had higher leptin levels and significant lower adiponectin levels.

Funding:
None.

Key-words: (up to 5):
Adipokines, Premature Birth, Infants, Small for Gestational Age.

Abstract #00004964 en

Prevalence of anemia and description of hematimetric index in Brazilian infants in relation to birth weight

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Vieira Erika (1), Luna Leonardo (1), Rosa Vitor Hugo (1), Strufaldi Maria Wany (1), Suano-Souza Fabíola (1) (1) School of Medicine/ Federal University of Sao Paulo

Background/aims:
Iron deficiency anemia in childhood is a global public health problem, affecting up to half of the population under 2 years of age. Latest Brazilian survey among children aged 6 to 23 months revealed 19% anemia prevalence with 7,9% iron deficiency anemia. Therefore, the objective of this study was to assess anemia prevalence and describe hematimetric index in infants in relation to birth weight.

Methods:
Cross-sectional multicenter study with infants with very low birth weight (VLBW)(n=27), low birth weight (LBW)(n=17) and normal birth weight (NBW)(n=43) from University hospitals and Basic Health Units in São Paulo/Brazil. Participants were assessed at a corrected age between 9 and 24 months, when data and blood samples were collected. Study was approved by the institution's Ethics Committee.

Results:
Groups were similar in gender and chronological age. Birth weight adequacy showed greater numbers of small for gestational age (SGA) in LBW ($p<0.001$). Exclusive breastfeeding duration and age of food introduction were similar. Total breastfeeding duration (months) was greater in NBW (10.95±6.44) compared to LBW (5.15±4.98) and VLBW (6.84±5.73) ($p<0.001$). Formula was earlier introduced in LBW ($p<0.05$). VLBW and LBW had higher rates of iron supplementation ($p<0.05$) and higher iron doses ($p<0.001$). Anemia prevalence was 7,4% in VLBW, 29,4% in LBW and 9,2% in NBW ($p<0.05$). Mean corpuscular hemoglobin concentration was lower while microcytosis was higher in LBW ($p< 0.05$).

Conclusions:
The highest anemia prevalence found in this study (29.4%) was in LBW. Despite the highest doses of iron supplementation, highest prevalence of SGA infants and shortest total breastfeeding duration suggest an important role of intrauterine growth and feeding in early life in development of anemia.

Funding:
None

Key-words: (up to 5):
Anemia, Iron-deficiency, Infants, Small for Gestational Age, Breastfeeding

Abstract #00004965 en

Comprehensive characterization of the left ventricular cardiac remodeling in rat after neonatal hyperoxia relevance for cardiomyopathy following prematurity

Impact of Early Life Exposures and Environmental Pollutants

De Sousa Do Outeiro Coraline (1), R Dartora Daniela (1), He Ying (1), Daniel Kate (2), Gaudet Chantal (2), Cloutier Anik (1), Luu Thuy Mai (1), Jankov Robert P (2), Nuyt Anne Monique (1)
(1) CHU Sainte-Justine Azrieli Research Center and Department of Pediatrics, Université de Montréal , (2) Department of Pediatrics, CHEO Research institute, Ottawa

Background/aims:
Prematurity (PT) is associated with lifelong increased risk of cardiovascular diseases. We showed that newborn rats transiently exposed to hyperoxia, mimicking PT-related conditions, develop Oxygen-induced cardiomyopathy (OIC) characterized by left ventricular (LV) remodeling. However, the effect of neonatal hyperoxia exposure over different LV components is unknown. We aimed to evaluate the impact of neonatal hyperoxia over different cellular components in OIC rats.

Methods:
Male Sprague-Dawley pups were kept with their mother in 80% O2 (OIC) or room air (Ctrl) from P3 to P10. At 4 and 16 weeks of age we used stereology to assess cardiomyocyte volume, and the density of fibroblasts, myofibroblasts, macrophages, and collagen in LV. Results (mean±SEM; Ctrl vs OIC) are compared using t test. Ethics (#2024-6844).

Results:
At 4 and 16 weeks, LV of OIC rats have increased cardiomyocytes volume (4wks: 6±0.5x10^3 vs 9±0.7x10^3 µm3; 16wks: 9±0.5 x10^3 vs 15±0.7 x10^3 µm3) and higher fibroblast (4wks: 63±2x10^5 vs 74±2x10^5 cells/cm3 ; 16wks: 47±2 x10^5 vs 58±3x10^5 cells/cm3), myofibroblast (4wks: 10±0.1x10^5 vs 21±1x10^5 cells/cm3 ; 16wks: 9±1x10^5 vs 15±1x10^5 cells/cm3) and macrophage density (4wks: 16±2.3x10^5 vs 44±1.8x10^5 cells/cm3 ; 16wks: 6±0.6x10^5 vs 11±0.8x10^5 cells/cm3) compared to Ctrl. Collagen deposition was increased at 16wks (0.02±0.02 vs 0.04±0.003).

Conclusions:
We showed that neonatal exposure to hyperoxia modulates different LV cellular populations in juvenile and adult OIC rats. These results reinforce the distinct cardiac alterations elicited by PT-related conditions and pave the way to enhance the mechanistic understanding of these changes and the long-term increased susceptibility to cardiac diseases following PT.

Funding:
(1) Fond de recherche du Québec, Santé (BF2-343016) ; (2) CHU Sainte-Justine Foundation

Key-words: (up to 5):
Prematurity ; Cardiac remodeling ; Cell population ; Stereology ; Hyperoxia

Abstract #00004966 en

The impact of transient neonatal exposure to hyperoxia on skeletal muscle resident fibro-adipogenic progenitors, relevance for preterm birth conditions

Impact of Early Life Exposures and Environmental Pollutants

Desaulniers Rébecca (1), Deprez Alyson (2), Cloutier Anik (2), De Dousa Do Outeiro Coraline (2), Poletto Bonetto Jessica (2), Nuyt Anne Monique (3), Dumont Nicolas (1)
(1) CHU Sainte Justine Research Center, Department Physiology, Université de Montréal, (2) CHU Sainte Justine Research Center, (3) CHU Sainte Justine Research Center, Department of Pediatrics

Background/aims:
Individuals born preterm (PT; < 37 weeks of gestation) display an increased risk of chronic disease and reduced exercise capacity in adulthood. Skeletal muscle, a key determinant of overall health, is at a critical phase of development at the time of PT. We have shown that newborn rats exposed to high oxygen (O2), mimicking PT-related conditions, display impaired muscle function, regeneration, and fibrosis. However, its mechanism in the latter remains unknown. Fibro-adipogenic progenitors (FAPs) are key mediators of fibrosis in the muscle. Thus, we hypothesize that transient neonatal hyperoxia exposure induces FAPs dysregulation, contributing to skeletal muscle impairment in PT-related conditions.

Methods:
Sprague-Dawley pups were kept with their mother in 80% O2 (OI - Oxygen Injury) or room air (CTRL) from days 3-10. Rats were sacrificed at 4 weeks. Fibrosis and FAPs subsets were assessed by immunofluorescence. ScRNA-seq was performed in the Tibialis Anterior (TA), cells isolated by FACs sorting, protein expression assessed by western blot. Results are mean ± SEM; OI vs Ctrl, compared using T-test, n=5-6/group. Ethics approved by CIBPAR (protocol #2023-5044).

Results:
TA from 4wks male rats display an increase in Pdgfra+ cells (pan-FAPs; 235 ± 15 vs 282 ± 35 cells/mm2) and a decrease of regenerative FAPs (TCF4+; 154 ± 21 vs 123 ± 20 cells/mm2). scRNAseq uncovered eight subclusters of FAPs with a shift towards an increased extracellular matrix modeling signature in OI, further validated by an increase in TGFβ expression (1.70 ± 0.210 vs 0.839 ± 0.163).

Conclusions:
FAPs phenotype is altered in vivo. Ongoing experiments consist of characterizing their behavior in vitro and validating these findings using human samples from a biobank of individuals born preterm. This project will lead to better understanding of muscle phenotype after preterm birth, and therapeutic avenues for a continuously growing population.

Funding:
1) Bourse de mérite de la faculté de médecine 2) Bourse d'excellence du CHU Sainte Justine

Key-words: (up to 5):
Prematurity, skeletal muscle, fibro-adipogenic progenitor, fibrosis, cell fate

Abstract #00004968 en

Furthering the integration of biological and social DOHaD models of inequities

Public Health Policies Across the Life Cycle.

MacGregor Megan (1), Massiris Miguel (2), Salvante Katrina (1), Delrieux Claudio (2), Nepomnaschy Pablo (1) (1) Faculty of Health Sciences, Simon Fraser University, (2) CONICET, Argentina - Universidad del Sur, Argentina

Background/aims:
Health inequities affect not only wellbeing but also socio-economic opportunities and, thus, are a critical part of ongoing social debates about structural poverty. As a result, a variety of social and biological models have emerged in an attempt to understand the origins, maintenance, and increase of health inequities. Differences in epistemological and methodological traditions between disciplines have hindered the integration of said biological and social models. Our field, DOHaD, tends to focus primarily on the biological mechanisms by which social exposures exert their effects, but rarely engages fully with social inequities models. On the other hand, social models tend to focus on upstream social determinants without exhaustive discussions of the biological mechanisms involved. That said, Nancy Krieger, author of the “Eco-social Theory of Disease Distribution”, the dominant model in social epidemiology, recently called for a much-needed life-course perspective. Specifically, Krieger highlights the importance of investigating the effects of the timing of social and physical exposures on the origin and maintenance of health inequities. This call represents an advance in the integration of social and biological models. Yet, social models still fail to fully consider the long-term consequences of the constraints and allowances of the biological mechanisms involved, including, for example, transgenerational effects. Here, we use Natural Language Processing and Knowledge Graphs to review the main models stemming from both, social and biological, disciplines, and propose paths for furthering their integration. We aim to contribute to the emergence of a synthetic model of the factors causing and perpetuating inequities within individuals and across generations. We hope that this model will help inform governments, the media, and the public and be used to improve upon current programs aimed at curbing the impacts of synergistic interactions between social and physical exposures that result in the perpetuation of health, social and economic inequities.

Methods:

Results:

Conclusions:

Funding:

Key-words: (up to 5):

Abstract #00004970 en

Modulation of GlcN-6-P synthase activity by metformin in rats with gestational diabetes and effects on the offspring

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Ortiz-Ramírez Jorge Armando (1), Lazo de la Vega Monroy Maria Luisa (1), Barbosa-Sabanero Gloria (1), López-Romero Everardo (2)
(1) Department of Medical Sciences, Division of Health Sciences, University of Guanajuato, (2) Department of Biology, Division of Natural and Exact Sciences, University of Guanajuato

Background/aims:
Gestational Diabetes Mellitus (GDM) affects both maternal and fetal health. Metformin is commonly used to control hyperglycemia during pregnancy. GlcN-6-P synthase, a key enzyme in the hexosamine pathway, plays a critical role in the O-GlcNAcylation cycle. However, the effects of metformin on this enzyme and offspring health remain underexplored. The objective was to evaluate placental GlcN-6-P synthase activity of rats with GDM and association with neonatal outcomes.

Methods:
Twenty Wistar rats (n=5 per group) were mated, pregnancy was confirmed by vaginal smear and mucous plug detection. The experimental groups were: control (Ctrl), control + metformin (Ctrl+Met), gestational diabetes mellitus (GDM), and GDM + metformin (GDM+Met). GDM was induced by administering nicotinamide (120 mg/kg) and streptozotocin (40 mg/kg). The Ctrl+Met and GDM+Met groups received oral metformin (50 mg/kg), while the other groups received the vehicle. On gestational day 18, placental tissue was collected, morphometric parameters were assessed, and GlcN-6-P synthase activity was evaluated using the Morgan-Elson method. Offspring weight, length, and abdominal diameter were measured. Statistical significance was set at $p < 0.05$. The study was approved by the Research Ethics Committee of the University of Guanajuato (CIBIUG-P49-2022).

Results:
GDM offspring had higher weight compared to controls and GDM+Met group ($p<0.0001$). Offspring from metformin-treated groups exhibited lower weight and size compared to controls ($p<0.0001$). GlcN-6-P synthase activity was lower in metformin-treated groups ($p<0.0001$) and higher in the GDM group compared to control ($p<0.0001$). A positive correlation was observed between placental GlcN-6-P synthase activity and birth weight.

Conclusions:
Metformin treatment in GDM reduces placental GlcN-6-P synthase activity, potentially modulating nutrient sensing pathways in the placenta and impacting fetal growth. These results underscore the need for further research to optimize GDM treatment strategies, improving maternal and fetal health.

Funding:
UG-CIIC-56/2023.

Key-words: (up to 5):
Placenta, GlcN-6-P synthase, Metformin.

Abstract #00004971 en

Maternal Plasma Fatty Acid Profile and its Association with Neonatal Adiposity: Prospective Cohort Study of Brazilian Puerperal Women and Infants

Mechanisms Determining Transgenerational Effects of Health and Disease

Ranquine Layla (1), Ferreira Carolina (1), Barbosa Agny Júlia (1), Pinto Gabriela (1), Moura Cintia (2), Bissoli Thaisa (2), Torres Alexandre (3), Rebelo Fernanda (2), El-Bacha Tatiana (1)
(1) Institute of Nutrition Josué de Castro, Federal University of Rio de Janeiro, (2) Fernandes Figueira Institute/Oswaldo Cruz Foundation, (3) Institute of Chemistry, Federal University of Rio de Janeiro

Background/aims:
An adequate lipid supply, in both quantity and quality, is essential for fetal and newborn growth. During lactation, maternal diet, body composition, and metabolic health influence the fatty acid content of human milk, potentially affecting infant health and development. This study aimed to assess the relationship between maternal plasma fatty acid profile and infant adiposity in the immediate puerperium of exclusively breastfed infants.

Methods:
This is an ongoing prospective cohort at the Fernandes Figueira Institute/Fiocruz, Rio de Janeiro, Brazil (CAAE: 26971319.1.0000.5269). Sixty-eight exclusive breastfeeding mother-baby dyads were included, and data and biological samples were collected up to 15 days postpartum. The maternal plasma fatty acid profile was analysed by gas chromatography with a flame ionisation detector and infant adiposity by air displacement plethysmography. Statistical analyses were performed using GraphPad Prism (version 9.5).

Results:
All pregnancies were at term (39.3 weeks (± 1.1 SD)) and infant anthropometry at birth was within the appropriate range. Forty-one fatty acids were identified (10-24 carbon length). Significant positive correlations with infant adiposity were found for 16:0 (r=0.27, p=0.05), 17:0 (r=0.29, p=0.04), 18:2n-6 (r=0.30, p=0.03), 20:2n-6 (r=0.29, p=0.04), 20:4n-6 (r=0.34, p=0.01), 22:0 (r=0.29, p=0.04), total polyunsaturated (r=0.28, p=0.04) and total n-3 (r=0.28, p=0.04) and n-6 (r=0.31, p=0.02) fatty acids.

Conclusions:
The significant correlation with palmitic (16:0), possibly a marker of maternal adiposity, highlights the importance of assessing gestational weight gain and pregestational BMI. Significant correlations with essential fatty acids underline the need for nutritional intervention strategies during pregnancy to prevent metabolic disorders that can impact their progeny in the short and long term.

Funding:
FAPERJ, CNPq, CAPES.

Key-words: (up to 5):
postpartum; maternal fatty acids; infant adiposity.

Abstract #00004977 en

Associations of prenatal exposure to acrylamide and risk of neurodevelopmental and mental disorders: A longitudinal biomarker-based study from Denmark

Impact of Early Life Exposures and Environmental Pollutants

Chandia-Poblete Damian (1), Tuffier Stephane (1), Vryonidis Efstathios (2), Halldorsson Thorhallur Ingi (3), Bjerregaard Anne Ahrendt (4), Strøm Marin (5), Rytter Dorte (6), Bech Bodil Hammer (6), Henriksen Tine Brink (7), Törnqvist Margareta (2), Olsen Sjurdur Frodi (4), Pedersen Marie (1)
(1) University of Copenhagen, (2) University of Stockholm, (3) University of Iceland, (4) Statens Serum Institut, (5) University of the Faroe Islands, (6) University of Aarhus, (7) University of Aarhus Hospital

Background/aims:
Exposure to acrylamide (AA) from diet and tobacco smoke during prenatal development is of concern as AA is neurotoxic. We aimed to assess the associations of prenatal exposure to AA with the incidence rates of the offsprings' neurodevelopmental and mental health disorders

Methods:
Prenatal exposure to AA was quantified through measurement of the hemoglobin adducts from AA (HbAA) in maternal blood samples from a Danish pregnancy cohort (N=996). Poisson models were fitted with incidence of attention deficit hyperactivity disorder (ADHD) and depression using diagnosis and/or prescription for medication and diagnosis only for autism spectrum disorder (ASD), anxiety, and any mental health disorders

Results:
Higher AA was associated with increased risk of anxiety with an IRR of 1.02 (0.98, 1.05) per 10-pmol/g Hb increase in HbAA after adjustment for smoking, education, and income. Among offspring of smokers, the IRR of developing anxiety was 2.22 (1.07, 4.91) for the highest exposed offspring compared with those exposed to AA levels lower than the median level. A corresponding IRR of 1.36 (1.01, 1.84) was observed for any diagnosis of mental disorder(s) when the highest exposed group was compared to the lowest exposure group. Higher prenatal exposure to AA were not found to be associated with increased risk of ASD, ADHD, and depression

Conclusions:
These preliminary findings suggest that prenatal exposure to AA increase the risk of developing anxiety, and any diagnosis of mental disorders in the offspring later in life

Funding:
This study has been prepared as part of the CHIPS project funded by the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 758151)

Key-words: (up to 5):
Biomarkers of exposure, Exposure assessment, Epidemiology, Neurodevelopmental outcomes, Mental health outcomes

Abstract #00004978 en

Metformin effects on placental GlcN-6-P synthase activity in women with gestational diabetes and neonatal outcomes

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Ortiz-Ramírez Jorge Armando (1), Lazo-de-la-Vega-Monroy Maria Luisa (1), Paulino-Gonzalez Angel David (1), Pantoja-Barroso Claudia Jimena (1), Villanueva-Tapia Leydi Arlete (1), López-Romero Everardo (2), Barbosa-Sabanero
Gloria (1)
(1) Department of Medical Sciences, Division of Health Sciences, University of Guanajuato, (2) Department of Biology, Division of Natural and Exact Sciences, University of Guanajuato

Background/aims:
Gestational diabetes mellitus (GDM) is the most common metabolic disorder during pregnancy, affecting both the mother and fetus. In women with GDM, the placenta is exposed to hyperglycemia, altering metabolic signaling pathways and key enzymes. Metformin, widely used during pregnancy, controls maternal hyperglycemia. However, the effect of metformin on GlcN-6-P synthase activity and on offspring health remain unknown. The objective was to evaluate GlcN-6-P synthase activity in placental tissue from women with GDM treated with or without metformin and its association with neonatal outcomes.

Methods:
A total of 36 pregnant women with a physiological pregnancy (Control), with GDM and GDM treated with metformin (GDM+Met) were recruited. Clinical and biochemical data from mothers and their newborns (NB) were collected. A placental tissue biopsy was taken, and GlcN-6-P synthase activity was measured by modified Morgan-Elson method. Statistical significance was set at $p < 0.05$. The study was approved by the corresponding research and ethics committees (folio number 15/2023, CEI 20-2023 and CIBIUG-P49-2022).

Results:
Women with GDM and GDM+Met had higher pregestational BMI ($p < 0.001$) compared to the Control group. HbA1c was higher in the GDM group ($p < 0.05$) compared to Control and GDM+Met groups ($p < 0.05$). Newborns in the GDM group had higher birth weight, length, and head circumference than the Control and GDM+Met groups ($p < 0.001$). GlcN-6-P synthase activity was higher in the GDM group compared to Control ($p < 0.0001$). In the GDM+Met group, enzyme activity was lower than in both Control and GDM groups ($p < 0.0001$). No significant differences in the enzyme activity were found based on neonatal sex.

Conclusions:
Metformin reduces GlcN-6-P synthase activity in the placenta, suggesting modulation of placental nutrient-sensing pathways with implications beyond maternal glucose control.

Funding:
This project was funded by University of Guanajuato UG-CIIC-105/2024, UG-CIIC-255/2024.

Key-words: (up to 5):
GDM, Placenta, GlcN-6-P synthase, Metformin

Abstract #00004980 en

Effects of Probiotic Supplementation in Obese Rat Mothers: Metabolic Benefits in Male and Female Young Adult Offspring.

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Prieto-Ibañez Vidblain (1), Esparza-Hurtado Natalia (1), Reyes-Castro Luis A. (1), Trejo-Estrada Sergio (2), Juárez-Pilares Gimena (3), Ibáñez-Chávez Carlos Alberto (4), Rodríguez-González Guadalupe Leticia (1), Valdéz-Trevizo Brandon Hassan (1), Soto-Martínez Javier Alejandro (1), Zambrano Elena (4)

(1) Departamento de Biología de la Reproducción, Instituto Nacional de Ciencias Médicas y Nutrición SZ, (2) Instituto Politécnico Nacional-Tlaxcala, (3) Depto Investigación Experimental y Bioterio, Instituto Nacional de Ciencias Médicas y Nutrición SZ, (4) Biol Reproducción, Instituto Nacional de Ciencias Médicas y Nutrición SZ/Facultad de Química,

UNAM

Background/aims:

Maternal obesity contributes to intestinal dysbiosis which can colonize the gastrointestinal tract of her progeny (F1) during pregnancy, delivery and lactation, with metabolic alterations and adipose tissue atrophy in a sex-specific manner. It's important to develop interventions to prevent offspring metabolic alterations induced by maternal obesity. We evaluated whether obese mothers' probiotic supplementation can ameliorate F1 adipose tissue expansion and metabolic dysfunction.

Methods:

Weaned female Wistar rats were fed a control (C) or high-fat diet to induce obesity (MO). One month before mating and throughout pregnancy and lactation, half of the rats were supplemented orally with a probiotic (1010 CFU/day): C, CP and MO (n=6); MOP (n=5). F1 was weaned on C diet and euthanized at 110 days. Body fat mass were evaluated by MRI and fat depots were excised to estimate adiposity index (AI). Retroperitoneal fat adipocyte size was modeled by gamma distribution. Serum glucose, triglyceride and insulin concentrations and insulin resistance index (HOMA-IR) were determined. All procedures followed institutional ethical guidelines. Analyses by two way-ANOVA.

Results:

MO male and female F1 had higher fat mass, AI, triglyceride, insulin and HOMA-IR than C, which were improved by MOP. MOP female had lower glucose and more small adipocytes than MO but similar than C. MO males and females had more large adipocytes than C, but MOP reduced them compared with MO. C and CP parameters were similar.

Conclusions:

Maternal probiotic supplementation of obese mothers, improves adipose tissue expansion in F1 by reducing hypertrophy in both male and female, and increasing small adipocytes in females. These changes were associated with an improvement in lipid profiles in both sexes and the restoration of glucose metabolism in females. Timely maternal probiotic intervention has sex-specific benefits for offspring metabolism.

Funding:

FONCICYT/49/2016.

Key-words: (up to 5):

Maternal obesity, dysbiosis, intervention, probiotic, adipose tissue.

Abstract #00004999 en

Consumption of ultra-processed foods and gut microbiota in the first two years: a systematic review.

Role of Infant and Young Child Feeding Practices on Long-Term Health

Damasio Faggiani Lucas (1), do Manco Machado Rafaela (1), Giacomini Isabel (1), Augusto Cardoso Marly (1) (1) University of São Paulo

Background/aims:
The first two years of life are fundamental for the establishment of the gut microbiota, with diet being one of the main early exposures. The consumption of ultra-processed foods (UPF) has increased considerably worldwide, including among young children. The present study aims to review scientific evidence on the effects of consuming UPF in the composition of the gut microbiota in the first two years of life.

Methods:
This study addressed the following research question using the PECO framework: (P)opulation: children aged 0–2 years; (E)xposure: UPF consumption; (C)omparator: no UPF consumption; (O)utcome—gut microbiota taxonomy and/or diversity parameters. A systematic literature search was conducted independently by two authors across PubMed, LILACS, SCOPUS, and Web of Science. Initial screening of titles and abstracts was performed using Rayyan software, with conflicts resolved by a third author. The exclusion criteria are absence of gut microbiota as outcome, absence of UPF, population with comorbidities, in vitro or animal models, humans older than 2 years of age and reviews. After full-text review of eligible studies, data extraction will be performed using a standardized electronic spreadsheet and verified by all authors.

Results:
Overall, 2124 articles were screened (891 PubMed, 572 ISI/Web of Science, 520 Scopus and 141 LILACS). After the exclusion of duplicates, 1458 articles remained for the first stage of study selection. Of them, 1384 articles did not meet the eligibility criteria, remaining 42 articles (98% agreement; Kappa 0.71): 35 observational studies and 7 clinical trials.

Conclusions:
Data from the included studies will be extracted into a standardized electronic spreadsheet, summarized in tables according to the study design, risk of bias and quality of evidence.

Funding:
Faggiani received doctoral scholarship from FAPESP (grant number 2024/18709-0). The founder had no role in the study design, data collection and analysis.

Key-words: (up to 5):
systematic review; diet; gut microbiota; child; public health.

Abstract #00005000 en

Do Different Adverse Intrauterine Environments Influence the Trajectory of BMI-for-Age Until Preschool Age?

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Koglin Gabriela (1), da Silva Clécio (2), Bandeira Denise (2), Valentini Nadia (2), Goldani Marcelo (2), Bernardi Juliana (2)
(1) UFRGS, (2) Universidade Federal do Rio Grande do Sul; Hospital de Clínicas de Porto Alegre

Background/aims:
This study aimed to assess whether adverse intrauterine environments influence the body mass index-for-age Z-score in preschool-aged children.

Methods:
This longitudinal study used a convenience sample of mothers and their newborns from three public hospitals in southern Brazil. Mother-child pairs were allocated into five intrauterine environment groups based on different maternal gestational clinical conditions: intrauterine growth restriction (IUGR), and a control group. Children's BMI/A Z-scores were assessed at seven time points, from birth to six months of age and again at preschool age. Data analysis was conducted using a regression model estimated through Generalized Estimating Equations. The study was approved by the Ethics Committees CEP/HCPA:
2011-0097 and 2017-0107, and CEP/GHC: 2011-027.

Results:
Initial assessments included 342 mother-child pairs, with 115 reassessed at preschool age. At birth, the IUGR group had significantly lower BMI/A Z-scores than other groups ($p<0.05$). Intra-group changes in BMI/A Z-scores showed a reduction from birth to 7 days in the DM group (0.0553; p=0.019), from birth to 15 days in the smoking (0.5345; p=0.027) and control groups (0.4328; p=0.038), an increase from 15 days to preschool age in the smoking group (-1.1803; p=0.025), from birth to preschool in the IUGR group (-1.277; p=0.01), from 7 days to preschool in the IUGR group (-1.4482; p=0.011), and a reduction from birth to 30 days in the control group (0.385; p=0.034).

Conclusions:
Children born to mothers with IUGR had lower BMI/A Z-scores at birth. However, by preschool age, this difference was no longer present, suggesting postnatal catch-up growth. The DM, tobacco, and control groups showed reductions in BMI/A Z-scores during the first weeks of life, but by preschool age, the tobacco group's BMI/A Z-scores had increased.

Funding:
FIPE - Hospital de Clínicas de Porto Alegre.

Key-words: (up to 5):
Fetal Programming. Preschool Child. Longitudinal Studies. Body Mass Index.

Abstract #00005002 en

Effect of metformin on the expression of glucose transporters in the placenta of gestational diabetes mellitus rats

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

wang jingxin (1), Mi Yang (1), Luo Xiao (1), Yang Huimin (1) (1)

Background/aims:
Aims: This study aimed to investigate the impact of metformin on placental parameters and glucose transporters (GLUTs) expression in gestational diabetes mellitus (GDM) rats.

Methods:
Methods: A GDM rat model was established by combining a high-fat diet with streptozotocin injection. The experiments were divided into the normal pregnancy, GDM group, insulin group, and metformin group. Fasting plasma glucose (FPG), maternal body weight, progeny parameters in GDM rats, and expression levels of GLUT1, 3, and 4 in the placenta were investigated. Furthermore, the correlation between placental GLUTs expression and placental and fetal parameters was analyzed.

Results:
Results: The FPG levels in the metformin group were significantly lower than those in the GDM group ($p < 0.05$). However, no significant differences were observed in body weight and fasting insulin (FINS) levels between the two groups. Placental weight was significantly higher in the metformin group than in the GDM group ($p < 0.05$), whereas no significant differences were observed in fetal weight and crown-rump length between the groups. Our analysis of placental GLUTs expression revealed that the metformin group exhibited significantly reduced GLUT1 expression compared to the GDM group ($p < 0.05$), whereas GLUT3 and GLUT4 expression levels were markedly elevated. Furthermore, correlation analysis demonstrated a negative association between placental GLUT3 expression and fetal weight in the GDM group.

Conclusions:
Conclusions: Oral metformin administration in GDM significantly improves FPG levels without inducing maternal weight gain during pregnancy. Metformin can upregulates the expression of GLUT1 and downregulating the expression of GLUT3 and 4 in placenta of GDM. Furthermore, correlation analysis suggest that altered GLUT expression levels may influence offspring metabolic development.

Funding:
The funding source for Shaanxi Province key research and development plan key industry innovation chain. The project name is the study of Risk factors screening and Prevention technology for Birth defects in Shaanxi Province based on the Western China Longitudinal mother-Child Cohort. The project number is 2021ZDLSF02-14.

Key-words: (up to 5):
Gestational diabetes mellitus; Metformin; Glucose transporters; Insulin; placenta

Abstract #00005005 en

Association of Leptin, Insulin, and Adiponectin in Breast Milk with the Trajectory of BMI-for-Age Z-Scores in Different Adverse Intrauterine Environments

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Koglin Gabriela (1), da Silva Clécio (2), Bandeira Denise (2), Valentini Nadia (2), Goldani Marcelo (2), Bernardi Juliana (2)

(1) Universidade Federal do Rio Grande do Sul, (2) Universidade Federal do Rio Grande do Sul; Hospital de Clínicas de Porto Alegre

Background/aims:

This study aimed to analyze the influence of leptin, insulin, and adiponectin concentrations in breast milk on the body mass index-for-age Z-score (BMI/A) in children who experienced adverse intrauterine environments during fetal life.

Methods:

This is a longitudinal study using a convenience sample of mothers and their newborns from three public hospitals in a state capital in the far south of Brazil. Mother-child pairs were divided into five groups according to different intrauterine environments based on maternal gestational clinical conditions: diabetes mellitus, systemic arterial hypertension, smoking, intrauterine growth restriction (small for gestational age newborns), and a control group. Children's weight, length, and Z-scores were measured at birth, and at 7, 15, 30, 90, 180 days, and during the preschool age. Breast milk was collected from mothers within the first 48 hours after birth and again at 30 days of infant age, when leptin, adiponectin, and insulin levels were quantified, and their variations between the two time points (delta) were calculated. The estimated linear regression model was developed using the Generalized Estimating Equations approach. The study was approved by the Ethics Committees of HCPA: 2011-0097 and 2017-0107, and GHC: 2011-027.

Results:

The delta of the evaluated peptides interacted with time [(leptin: Wald χ^2 = 49.770; p<0.001), (adiponectin: Wald χ^2 = 16.481; p=0.011), (insulin: Wald χ^2 = 20.752; p=0.002)], positively or negatively affecting the BMI/A Z-score at different time points. The influence of the delta on the BMI/A Z-score varied among intrauterine environment groups [(leptin: Wald χ^2 = 31.099; p<0.001), (adiponectin: Wald χ^2 =
43.875; p<0.001), (insulin: Wald χ^2 = 43.105; p<0.001)].

Conclusions:

Time and its interaction with leptin delta influenced the behavior of BMI/A Z-scores in the studied population, with differences observed among the intrauterine groups.

Funding:

FIPE - Hospital de Clínicas de Porto Alegre.

Key-words: (up to 5):

Fetal Programming. Preschool Child. Longitudinal Studies. Body Mass Index. Breast Milk.

Abstract #00005008 en

The impact of blastomere loss during frozen-thawed embryo transfer on the physical and neurocognitive development of offspring in childhood

Interventional strategies to prevent late-life outcomes resulting from early-life insults

He Yi-Chen (1), Dong Ze-Han (2), Li Cheng (1), Qin Ning-Xin (3), Liu Han (1), Wu Yan-Ting (1), Huang He-Feng (1)
(1) Obstetrics and Gynecology Hospital, Fudan University, Shanghai, China , (2) School of Medicine, Shanghai Jiao Tong University, Shanghai, China, (3) Shanghai First Maternity and Infant Hospital, Tongji University, Shanghai, China.

Background/aims:
Despite the common issue of blastomere loss in frozen-thawed embryo transfer (FET), little is known of the long-term impact on offspring conceived from FET with blastomere loss. The aim of the present study is to evaluate the effect of blastomere loss in FET on the physical and neurocognitive development of offspring in childhood.

Methods:
This prospective cohort study included 145 singleton offspring aged 1.5-4 years old born after FET in Shanghai. Demographic and reproductive characteristics, pregnancy and perinatal information were collected through clinical medical systems and questionnaires. Physical development status was evaluated in z-scored anthropometric outcomes. Neurocognitive development was assessed by Gesell Developmental Scale (GDS), which covered five domains of gross motor, fine motor, adaptability, language, and sociability.

Results:
A total of 15 children from the blastomere loss group and 130 children from the intact embryo group were followed up and evaluated. There was no significant difference in anthropometric outcomes of physical growth between the two groups. However, children from the blastomere loss group were at an increased risk of deficient in neurocognitive development including adaptability (adjusted OR=52.03, 95%CI 5.16-524.50, p=0.001) and language (adjusted OR=11.22, 95%CI 2.81-44.82, p=0.001), without sex discrepancy. No significant difference was found in the risk of developmental delay in gross motor (P =
0.075), fine motor (P = 0.531), and sociability (P = 0.121) between the two groups.

Conclusions:
The blastomere loss following FET is associated with neurocognitive development delay, particularly in adaptability and language, which needs further concern in assisted reproductive technology strategies.

Funding:
The Clinical Research Plan of Shanghai Shenkang Hospital Development Center (SHDC12018X17), The National Key Research and Development Program of China (2021YFC2700701, 2021YFC2701601)

Key-words: (up to 5):
Blastomere loss, Frozen embryo transfer, Neurocognitive development, Physical Development, Offspring

Abstract #00005015 en

Umbilical Cord Blood Vitamin D Level and Risk of Developing Asthma at Age 5 Years

Big Data and Cohorts in DOHaD Research.

Hara Chisato (1), Shibata Ryohei (2), Nakano Taiji (3), Yamaide Fumiya (4), Shimojo Naoki (5), Sakurai Kenichi (6)
(1) Graduate Schol of Medical and Pharmaceutical Sciences, Chiba University, (2) Department of Pediatric Surgery, Graduate School of Medicine, Chiba University, (3) Department of Pediatrics, Graduate School of Medicine, Chiba University, (4) Department of Pediatrics, International University of Health and Welfare Narita Hospital, (5) Center for Preventive Medical Sciences, (6) Center for Preventive Medical Sciences, Chiba University

Background/aims:
Vitamin D is involved in fetal immune development. As a marker of fetal vitamin D status, cord blood 25-hydroxyvitamin D [25(OH)D] has gained interest in relation to early immune outcomes. Accumulating evidence suggests that lower cord blood 25(OH)D levels are associated with an increased risk of respiratory infections and early wheezing. However, little is known about the association of cord blood 25(OH)D levels with the risk of developing asthma. This study aimed to examine the association between cord blood 25(OH)D levels and asthma diagnosis at age 5 years.

Methods:
A total of 306 pregnant women were enrolled in the Chiba High-risk Birth Cohort for Allergy (CHIBA) study, which targeted children with a parental history of allergy. Among them, 194 dyads with available cord blood and asthma diagnosis data at age 5 years were analyzed. Total 25(OH)D (sum of 25(OH)D_2 and 25(OH)D_3) levels were measured using liquid chromatography–tandem mass spectrometry. Asthma was diagnosed by a pediatric allergist based on the Japanese Guideline for Childhood Asthma 2014. Cases classified as suspected asthma were defined as having asthma-like symptoms without meeting the full diagnostic criteria. The associations of cord blood 25(OH)D levels with risks of developing asthma were determined by a multinomial logistic regression model, adjusting for season of birth, maternal smoking exposure, and maternal asthma history.

Results:
The mean cord blood 25(OH)D level was 6.3 ng/mL (SD ± 2.8 ng/mL). Of the 194 children, 21 were diagnosed as asthma, and 23 were diagnosed as suspected asthma at age 5 years. Higher cord blood 25(OH)D levels were associated with lower odds of developing asthma, compared to children without an asthma diagnosis (adjOR per 1.0 ng/mL increment = 0.801; 95%CI: 0.635–1.01).

Conclusions:
Our findings suggest that fetal vitamin D status is associated with the development of asthma in early childhood.

Funding:
This study was funded by AMED-Innovative Advanced research and Development Support (AMED-CREST) grant J17JK00058 and was partially supported by The Japan Health Foundation. This study was conducted with funds provided by RIKEN based on the Joint Research agreement between Chiba University and RIKEN.

Key-words: (up to 5):
vitamin D, cord blood, childhood asthma, fetal immune development, prenatal exposure

Abstract #00005017 en

Treatment with Humanin analog (HNG) prevents increased matrix metalloproteinase (MMP)-2 activity and vascular remodeling induced by neonatal exposure to hyperoxia

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Blascke de Mello Marcela Maria (1), De Sousa Do Outeiro Coraline (2), Maxence Girault Sotias Pierre Emmanuel (2),
Deprez Alyson (2), Cloutier Anik (2), Mai Luu Thuy (3), Ravizzoni Dartora Daniela (2), Mazzaron de Castro Michele (1), Nuyt Anne Monique (2)
(1) Ribeirao Preto Medical School, University of Sao Paulo, (2) CHU Sainte-Justine Research Center, Université de Montréal, (3) CHU Sainte-Justine, Université de Montréal

Background/aims:
Preterm birth (PT) is associated with increased risk of cardiovascular diseases. Altered vascular development is a key component of PT complications. Using a clinically relevant rat model mimicking PT-conditions, we previously showed reduced aortic elastin/collagen ratio associated with increased rigidity and, also cardiomyocyte remodeling and mitochondria (mito) dysfunction. Moreover, PT individuals present decreased circulating levels of humanin, a mito-derived and anti-apoptotic peptide. Whether changes in mito and humanin levels are also present in aorta are unknown. Thus, we aimed to evaluate whether neonatal treatment with HNG (humanin analog) could prevent arterial alterations caused by transient neonatal hyperoxia exposure in juvenile and adult rats.

Methods:
Male rat pups and their mother were kept in 80% O2 (OI) or room air (Ctrl) from postnatal days (P)3 to P10 and concomitantly treated subcutaneously with HNG (4 mg/kg/day) or vehicle (VHL). At 4 or 16 weeks, aortas were collected to perform gelatin zymography and hematoxylin-eosin staining (Ethics Committee #1385/2024). Results were expressed as mean ± SEM and statistical analysis was performed by Two-way ANOVA followed by Tukey post-test ($p<0.05$).

Results:
At 4 wks, neonatal hyperoxia did not induce vascular remodeling or alterations in MMP-2 activity in OI vs Ctrl. However, at adult (16wks) OI rats, there is increased aortic cross-sectional area (CSA; n=7-8; $p<0.05$) and media to lumen ratio (M/L; n=7-8; $p<0.05$) that were prevented by neonatal treatment with HNG. MMP-2 activity was also increased at 16 wks in the OI rats (n=5-6; $p<0.05$) and treatment with HNG seemed to prevent it (n=5-6; $p=0.06$).

Conclusions:
Adult (16 wks) rats transiently exposed to neonatal hyperoxia exhibited increased MMP-2 activity and aorta hypertrophic remodeling. Neonatal treatment with HNG seems to prevent these alterations.

Funding:
FAPESP, CNPQ, CAPES, CIHR, CRC and Foundation Sainte-Justine.

Key-words: (up to 5):
Preterm Birth; Hyperoxia; MMP-2; Arterial remodeling; Humanin.

Abstract #00005019 en

Future Finland – the Birth of a New Finnish Nationwide Birth Cohort

Big Data and Cohorts in DOHaD Research.

Kajantie Eero (1)
(1) Finnish Institute for Health and Welfare and University of Oulu

Background/aims:
Birth cohorts are invaluable to assess lifelong outcomes of prenatal and neonatal conditions. However, findings have limited generalisability to other generations. Moreover, existing birth cohorts have limitations: many mother-child cohorts ignore fathers/other parents and siblings, and few devote effort into inclusion of minorities.

We present the Future Finland Birth Cohort (FFBC), funded by the Finnish Cultural Foundation to create a data source enabling interdisciplinary research and intervention setups to promote population welfare.

Methods:
FFBC will comprise two arms:
1) National registers and other nationally collected data:
A nationwide register-linkage study of all people born in Finland during 2025-2029 (n>200,000), their parents and siblings. In addition to well-established healthcare registers (e.g. Medical Birth, Death, Medication and Patient registers), FFBC will harmonise data collected in structured format in routine antenatal and child healthcare and education, availability of which has been hindered by diversity of electronic records software.
2) In-depth data collection:
A subset of pregnant women will be invited during first trimester ultrasound to in-depth data collection including blood samples (first trimester, cord blood and newborn blood spot) and questionnaires to both parents, piloted regionally in 2025-2027 and extended nationwide by 2028.

Results:
FFBC data will be made available to the global scientific community for well-justified research purposes.

Conclusions:
FFBC is a new national birth cohort currently transferring from design to pilot phase. Unique features include (i) extensive secondary use of new forms of nationwide administrative data, (ii) linkage of parents and siblings, and (iii) combination of these with biological samples and questionnaires.

Funding:
Finnish Cultural Foundation

Key-words: (up to 5):
Birth cohort, national, register data, comprehensive, pregnancy

Abstract #00005020 en

What enablers and barriers influence breastmilk feeding in very preterm infants in Aotearoa New Zealand?

Role of Infant and Young Child Feeding Practices on Long-Term Health

Delgado Páramo L (1), Nickerson T (2), Bloomfield FH (1), Alexander T (1), Cormack B (1), Edmonds L (3), Kremer L (4), Ward K (5)

(1) Liggins Institute, University of Auckland, (2) Starship Children's Hospital, Auckland, (3) Victoria University of Wellington, (4) He Rau Kawakawa (School of Pharmacy), Ōtākou Whakaihu Waka (Otago University), Dunedin, (5) School of Nursing, University of Auckland, Auckland, New Zealand

Background/aims:

Worldwide, 11% of infants are born preterm and face lifelong increased risks for neurodisability, cardiometabolic disease and mortality. Breastmilk feeding is recognised as crucial to these infants' outcomes. In Aotearoa New Zealand (NZ), Māori (Indigenous people of Aotearoa) do not have equity in preterm birth rates and breastfeeding outcomes. We aimed to identify factors influencing breastmilk feeding in very preterm infants in NZ neonatal intensive care. We focused on understanding parents' lived experiences and how care received influenced their breastfeeding aspirations.

Methods:

We conducted qualitative semi-structured interviews with parents of infants born <34 weeks' gestation and healthcare professionals involved in their care, and collected quantitative data from hospital records.
Interview data were analysed thematically using NVivo. Participants gave written consent (HDEC #16690).

Results:

To date, we have interviewed 21 parents and 12 healthcare professionals. Preliminary analysis indicates that despite pumping being exhausting and isolating mothers were determined and pressured themselves to express milk, viewing this as dutiful. Participants identified partners as essential for emotional and practical support. Connection and communication with staff, where parents felt empowered and participated in their infants' care and decision-making, was reported as important for bonding and confidence. Whānau Māori (n=4) transcripts are yet to be analysed, and an intentional Indigenous analysis will be completed prior to presenting. Staff also identified knowledge gaps about the importance of early breastmilk expression after preterm birth and about cultural competency and safety, and health equity.

Conclusions:

Maternal determination to pump supports breastmilk feeding, though it causes significant stress and parental isolation. Fostering breastfeeding self-efficacy, tailored communication and addressing staff knowledge gaps might improve fulfilment of breastfeeding aspirations in preterm infants' parents. This study highlights the importance of family-centred, culturally safe care to fulfil breastfeeding aspirations and improve health outcomes of preterm infants.

Funding:

NZ Health Research Council #22/736

Key-words: (up to 5):

Breastfeeding, preterm, neonate, breastmilk, NICU

Abstract #00005024 en

The roles of perceived stress and engagement in community cultural activities in the multigenerational effects of Indian Residential Schools on psychological in the children and/or grandchildren of former attendees

Mechanisms Determining Transgenerational Effects of Health and Disease

Bombay Amy (1)
(1) Department of Neuroscience, Carleton University

Background/aims:
Using the Indian Residential School (RS) system as an example of a collective trauma faced by large proportions of First Nations children across Canada for over a century from the mid-1800s until the 1990s, we will assess how the multigenerational effects of multiple adverse childhood experiences in former RS attendees may be changing over time in different age groups. It was also of interest to assess if greater levels of perceived stress among descendants of RS Survivors contribute to their symptoms of anxiety/depression, and if cultural engagement may protect against these negative generational effects.

Methods:
Analyses of the First Nations Regional Health Survey that collected data in First Nations communities across Canada assessed how parent and/or grandparent RS attendance is associated with symptoms of anxiety and depression (K-10) in First Nations youth and adults (ages 12 and older) in 2002/03, 2008/10, and 2015/16. Analyses also assessed if perceived stress and/or engagement in community cultural practices mediated and/or moderated the associations between parent and/or grandparent RS attendance and symptoms of anxiety/depression.

Results:
Despite the passage of time since the residential school era, significant multigenerational effects remain across time points, with high stress levels serving as a key mediator in predicting the increased anxiety and depression among the children and grandchildren of former RS attendees across different age groups. That said, those who more frequently participated in community cultural events were somewhat buffered against these negative effects in relation to psychological distress.

Conclusions:
The RS system in Canada has resulted in long-lasting multigenerational effects in the children and grandchildren of those who attended, including higher levels of perceived stress and psychological distress. Culture-based and trauma informed interventions should be provided to First Nations populations who have been harmed by past government assimilation policies that harmed generations of children.

Funding:
Canadian Institutes of Health Research

Key-words: (up to 5):
Multigenerational trauma, Indian Residential Schools, Collective trauma, Anxiety, Depression, Stress,
Cultural engagement

Abstract #00005026 en

Hypothalamic-pituitary-adrenal axis activity, metabolic energy, and the timing of menarche among a group of Mayan adolescent girls

Mechanisms Determining Transgenerational Effects of Health and Disease

Rowlands Amanda (2), Salvante Katrina G. (2), Nepomnaschy Pablo A. (2)
(2) Simon Fraser University

Background/aims:
Adolescence is a critical transition in which girls face energetic trade-offs between growth and reproductive development. These trade-offs can affect the onset and pace of this transition. The hypothalamic-pituitary-adrenal axis (HPAA) has been proposed as a modulator of metabolic energetic trade-offs, yet, few studies have examined its mechanistic role during girls' reproductive maturation.
Hypothesis: The HPAA modulates metabolic energy allocation and, thus, the pace of reproductive maturation. We predict that HPAA activity, somatic growth and energy uptake and storage levels should be linked to the timing of menarche.

Methods:
We used data from 29 pre-menarche Mayan adolescent girls from Guatemala, who also provided age at menarche data. We evaluated biomarkers of HPAA activity (cortisol), energy uptake (c-peptide), energy storage (adiponectin), and measures of height growth (proportion of final height), as predictors of timing of menarche.

Results:
The relationship between menarche timing and adiponectin depended on cortisol levels. At high cortisol levels pre-menarche, high adiponectin levels (lower fat stores) were associated with more time remaining to menarche relative to low adiponectin levels (higher fat stores). At low cortisol levels pre-menarche, high levels of adiponectin were associated with significantly shorter time remaining to menarche. For each 1% increase in proportion of their final height, girls were 1.34-months closer to reaching menarche.

Conclusions:
As predicted, time to menarche and energy levels were a function of HPAA activity, which was also linked to the pace of somatic growth. These findings suggest that earlier in the transition, energy mobilized from storage by the HPAA was mostly allocated towards growth. Future studies including the longitudinal collection of anthropometric and biomarker data throughout the adolescent transition should further explore within-individual changes in HPAA activity, energy levels, somatic growth, and reproductive maturation, to further clarify the HPAA's role in the transition.

Funding:
Doctoral Vanier Canada Graduate Scholarship; NSERC Discovery Grant (RGPIN-2018-06750).

Key-words: (up to 5):
Adolescence; reproductive maturation; menarche; hypothalamic-pituitary-adrenal axis; metabolic energy

Abstract #00005030 en

Association between maternal body composition and fetal adiposity

Mechanisms Determining Transgenerational Effects of Health and Disease

Ramos-Silva Tamiris (1), Alves Luzia Liania (1), Falcão de Carvalho Letícia (1), Pinheiro-Castro Natália (1), Oliveira Aires Isabel (1), Pereira Lopes Aldaísa (1), Antônia Rodrigues Martins Francilany (1), Domingos Biagio Leonardo (1), Louro Silva Paula (1), Helen de Carvalho Rondó Patrícia (1)
(1) University of São Paulo

Background/aims:
Fetal adiposity is a sensitive marker of intrauterine growth and early metabolic programming. Although maternal body mass index (BMI) is widely used, it shows high specificity but low sensitivity for detecting excessive body fat. This study aimed to evaluate the association between maternal fat mass (FM) and fat-free mass (FFM) in early pregnancy and fetal adiposity in the third trimester.

Methods:
A cross-sectional study was conducted with 1468 pregnant women receiving care at 37 Primary Health Care Units in Araraquara, Brazil. Women with gestational age (GA) <19 weeks were included; those with multiple pregnancies, diabetes, hypertension, HIV, bariatric surgery, or fetal congenital anomalies were excluded. All participants gave written consent (Ethics Committee nº 1.885.874) Sociodemographic and obstetric data were collected via standardized questionnaires. Maternal FM and FFM were assessed using segmental bioimpedance before 19 weeks of gestation. Fetal adiposity was measured by ultrasound after 29 weeks, including subcutaneous tissue of the abdomen (STA), arm fat area (AFA) and thingh fat area (TFA). Associations were tested using linear regression adjusted for GA.

Results:
Median maternal BMI, FM and FFM were 25.5 kg/m² 22.2 kg, and45.0 kg, respectively mean GA:13.7 weeks. Mean fetal STA, AFA, and TFA were 3.83 mm, 3.44 mm, and 6.07 mm, respectively (mean GA: 33.1 weeks). FM was positively associated with AFA and TFA ($p<0.001$). FFM was positively associated with STA ($p=0.004$), AFA, and TFA ($p<0.001$).

Conclusions:
Both maternal fat and fat-free mass were associated with fetal adiposity, particularly peripheral fat, from early pregnancy. These findings support the early identification of excessive fetal growth and may guide timely interventions to improve maternal-fetal health.

Funding:
São Paulo Research Foundation (FAPESP) (grant number 2015/03333–6, 2023/02404-3).

Key-words: (up to 5):
adiposity fetal; maternal fat mass; fat-free mass; bioimpedance; ultrasound.

Abstract #00005032 en

Adherence, Number of Consultations, and Initiation of Prenatal Care Among Pregnant Women in the Amazon Region

Public Health Policies Across the Life Cycle.

Freire Goncalves Danielle (1), da Silva Ferreira Elisangela (2), Pereira Rodrigues Diego (3), Jaime Castanheira Juliana (2), Beatriz Souza da Silva Anna (2)
(1) Universidade federal do pará, (2) Universidade Federal do Pará, (3) Universidade Federal Fluminense

Background/aims:
Prenatal care is a fundamental moment for welcoming and monitoring pregnant women, encompassing multidisciplinary clinical consultations, ordering and evaluation of exams, health education, and planning for childbirth, postpartum, and family planning. It is the main mechanism to reduce complications during pregnancy and the postpartum period. According to the Brazilian Ministry of Health, prenatal care should begin as early as possible, ideally by the 12th week of gestation, and should include at least six consultations. This study aims to describe prenatal care adherence among postpartum women treated at a public maternity hospital in the Amazon region.

Methods:
This is a descriptive, documentary, and quantitative study conducted in a referral maternity hospital for high-risk pregnancies in the Brazilian Amazon. Data were collected from medical records of postpartum women who gave birth in 2022 and 2023. According to calculations made using the SurveyMonkey online tool, with a 5% margin of error and a 95% confidence level, the sample consisted of 399 medical records out of a total of 16,987 births. Data were analyzed using descriptive statistics.

Results:
Among the medical records analyzed, the vast majority (92.2%) of the pregnant women had at least one prenatal consultation. However, only 131 (32.8%) completed six or more consultations. Regarding the initiation of prenatal care, 195 women (53%) began in the first trimester of pregnancy, while 105 (28.8%) initiated care only in the second trimester.

Conclusions:
High adherence to prenatal care was observed among the study participants. However, only a minority met the minimum number of consultations and began follow-up within the timeframe recommended by the Ministry of Health, highlighting inequalities in obstetric care for the studied population.

Funding:

Key-words: (up to 5):
Cuidado prenatal; política pública en salud; adherencia

Abstract #00005033 en

Access of Parturient Women Residing in the Amazon Region to Specialized Health Services

Public Health Policies Across the Life Cycle.

Freire Goncalves Danielle (1), da Silva Ferreira Elisangela (2), Pereira Rodrigues Diego (3), Juliana da Silva Silva Kalinda (2), Fraga Dias Roberta (2)
(1) Universidade federal do pará, (2) Universidade Federal do Pará, (3) Universidade Federal Fluminense

Background/aims:
The state of Pará covers a territorial area of 1,248,000 km² and is divided into 144 municipalities. The Metropolitan Region of Belém comprises eight municipalities and represents less than 1% of the state's territory. Given this vast geographic area and the high population density in inland regions, the discussion of public health access policies is essential. This study aims to describe the geographical origin of parturient women admitted for delivery in a referral maternity hospital for high-risk obstetrics in the Brazilian Amazon region.

Methods:
This is a descriptive, documentary, and quantitative study conducted in a referral maternity hospital for high-risk pregnancies in the Brazilian Amazon. Data were collected from medical records of postpartum women who gave birth in 2022 and 2023. Based on calculations using the SurveyMonkey online tool, with a 5% margin of error and 95% confidence level, the sample consisted of 399 medical records out of a total of 16,987 births. Data were analyzed using descriptive statistics.

Results:
The study found that 208 (52.1%) of the parturient women came from the Metropolitan Region of Belém, while 191 (47.9%) were from the interior of the state of Pará, highlighting a significant number of women from remote areas receiving care at the maternity hospital. Some parturient women were residents of municipalities such as Xinguara, Canaã dos Carajás, and Paragominas, located 780 km, 761 km, and 303 km from Belém, respectively.

Conclusions:
A significant proportion of parturient women originated from inland regions, many of whom traveled long distances to access care. These findings underscore the need to ensure healthcare access beyond the major urban center. The data reflect regional inequalities in access to specialized obstetric services.

Funding:

Key-words: (up to 5):
acceso a la salud; interiorización; desigualdad regional.

Abstract #00005035 en

Sociodemographic, Clinical, and Obstetric Profile of Postpartum Women in a Public Maternity Hospital in the Amazon Region

Public Health Policies Across the Life Cycle.

da Silva Ferreira Elisangela (1), Freire Goncalves Danielle (2), Pereira Rodrigues Diego (3), Rodrigues Silva Julieta (1), Késsia Pacheco de Almeida Oliveira Adrielle (1)
(1) Universidade Federal do Pará, (2) Universidade federal do pará, (3) Universidade Federal Fluminense

Background/aims:
Understanding the sociodemographic profile of postpartum women cared for in maternity hospitals is fundamental to gaining insight into the population served. This knowledge is essential for planning comprehensive care and organizing quality healthcare based on the specific and unique characteristics of this population. This study aims to describe the sociodemographic, clinical, and obstetric profile of postpartum women at a public maternity hospital in the Amazon region.

Methods:
This is a descriptive, documentary, and quantitative study conducted in a referral maternity hospital for high-risk obstetric cases in the Brazilian Amazon. Data were collected from medical records of postpartum women who gave birth in 2022 and 2023. According to the SurveyMonkey online calculator, with a 5% margin of error and a 95% confidence level, the sample consisted of 399 medical records out of a total of 16,987 births. The data were analyzed using descriptive statistics..

Results:
The predominant age group was 19 to 34 years (74.7%). Most had completed secondary education (46.6%), identified as homemakers (56%), resided in the Metropolitan Region of Belém (52.1%), were primigravida (41.4%), had undergone prenatal care (92.2%), and 32.8% had at least six prenatal consultations.

Conclusions:
The postpartum women showed adequate indicators in terms of age, education level, and number of prenatal visits. However, disparities in access and fragmentation of health services in the region were observed.

Funding:

Key-words: (up to 5):
Health profile; Postpartum women; Epidemiology; Maternity; Prenatal care

Abstract #00005040 en

Double burden of malnutrition in the mother-child pair: A latent transition analysis in the first 2 years of life

Public Health Policies Across the Life Cycle.

Zani Rodrigues Caroline (1), Cogo-Moreira Hugo (2), de Araújo Damasceno Ana Alice (3), Augusto Cardoso Marly (1), Hatzlhoffer Lourenço Bárbara (1)
(1) School of Public Health / University of São Paulo, (2) Department of Education, ICT and Learning / Østfold University College, (3) Multidisciplinary Center / Federal University of Acre

Background/aims:
The double burden of malnutrition (DBM) affects child development and health. This study aimed to classify mother-child pairs into groups of multiple malnutrition indicators during the first 2 years, and to assess the transition probabilities between groups over time.

Methods:
This analysis is part of the Maternal and Child Health and Nutrition in Acre, Brazil (MINA-Brazil Study), a population-based birth cohort in the Amazon region. Nutritional status of mother-child pairs was assessed at 1- and 2-year follow-ups using maternal BMI and WHO growth standards (height-for-age [HAZ] and weight-for-age [WAZ] Z-scores), hemoglobin, ferritin, vitamins A and D concentrations measured from child blood samples. Latent profile analysis identified malnutrition groups at each follow-up. Latent transition analysis estimated probabilities of transition between groups over time. Human ethical considerations were met.

Results:
At the 1-year follow-up, five mother-child profiles were identified: “adequate pair” (n=495, 51%) with all indicators within recommended cut-offs; “low HAZ/WAZ children” (n=240, 25%); “high HAZ/risk of overweight (ROW) children” (n=152, 16%); “anemia/iron deficiency children” (n=66, 7%); “high HAZ/WAZ and iron deficiency (DBM) children” (n=18, 2%). At the 2-year follow-up, three profiles emerged: “maternal overweight (OW)” (n=559, 58%); “low HAZ/WAZ children” (n=254, 26%); “OW pair” (n=158, 16%). For the “adequate pair” and “low HAZ/WAZ children” groups at 1 year, transition probabilities were 100% to “maternal OW” and “low HAZ/WAZ children” at 2 years, respectively. “High HAZ/ROW children” had an 88% probability to transition to “OW pair” and 12% to “maternal OW”. Probabilities of “anemia/iron deficiency children” transitioning to “maternal OW” and “low HAZ/WAZ children” were 63% and 32%, respectively. All “DBM children” transitioned to “OW pair” at 2 years.

Conclusions:
Distinct mother-child nutritional profiles were observed in the first 2 years, with notable transitions over time. Early DBM screening should be considered in this critical window in early life for health promotion.

Funding:
This work is part of the MINA-Brazil Study, which is supported by the São Paulo Research Foundation, FAPESP (grants #2016/00270-6 and #2022/03136-0). Rodrigues received scholarships from FAPESP (grants #2022/13550-8 and #2023/17875-1). Organizations involved in the financial support of this work had no role in the design, analysis, or writing of this abstract.

Key-words: (up to 5):
double burden of malnutrition; mother-child pair; overweight; growth faltering; micronutrient deficiencies.

Abstract #00005041 en

Resveratrol in the pre-gestational, pregnancy and lactation phases reduces MMP-2 activity, vascular dysfunction and hypertension in adult offspring

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Oliveira Ruan (1), Blascke de Mello Marcela Maria (1), Gomes Beatriz (1), Dourado Thales (2), Assis Victor (1), Tirapelli Carlos (2), Castro Michele (1)
(1) Ribeirao Preto Medical School / University of Sao Paulo, (2) Ribeirao Preto School of Pharmaceutical Science / University of Sao Paulo

Background/aims:
Vascular alterations of hypertension are associated with increased matrix metalloproteinases (MMP)-2 activity, which is activated by oxidative stress (ROS). Antioxidants reduce ROS and MMP-2 activity in hypertension, improving vascular dysfunction and remodeling. Treatment of spontaneously hypertensive rats (SHR) dams with resveratrol in pregnancy improved endothelial dysfunction and hypertension in their adult offspring. However, the mechanisms involved in the effects of resveratrol on adult offspring remain to be elucidated. We aimed to assess whether treatment with resveratrol in the pre-gestational, gestational and lactation reduces increased ROS and MMP-2 activity, thus reducing arterial hypertrophic remodeling and dysfunction, and hypertension in adult offspring.

Methods:
Wistar Kyoto (WKY) and SHR couples were treated with resveratrol (4g/kg) for 14 days before pregnancy. Resveratrol was continued in females during gestation and lactation, and was ceased. Female and male offspring were analyzed when reached 12 weeks of age. Systolic blood pressure (SBP) was analyzed by tail-cuff plethysmography from 8 until 12 weeks, and aortas were collected to perform gelatin and in situ zymography, DHE, vascular reactivity and H&E staining. Statistical analysis was performed by one-way ANOVA and Tukey post-test or t-test when appropriate ($p<0.05$).

Results:
Treatment with resveratrol in the SHR dams decreased SBP and ROS in the aortas of adult female SHR offspring ($p<0.05$). Accentuated aortic MMP-2 activity in the adult SHR offspring was decreased by resveratrol in both genders ($p<0.05$). Resveratrol seems to improve vascular function and hypertrophic remodeling in adult SHR offspring ($p<0.05$). However, adult female WKY offspring that received resveratrol from dams had increased aortic ROS and MMP-2 activity in addition to hypertrophic remodeling and dysfunction ($p<0.05$).

Conclusions:
Treatment of hypertensive dams with resveratrol in preconception, gestation and lactation improved hypertension-induced vascular hypertrophy and dysfunction in their adult offspring through decreasing oxidative stress and MMP-2 activity.

Funding:
FAPESP, CNPQ, CAPES

Key-words: (up to 5):
Pregnancy; MMP-2; Resveratrol; Hypertension; Arterial remodeling

Abstract #00005042 en

The effects of in vitro fertilization on maternal cardiovascular system

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Chukwuefe Henrietha (1), Chen Yutong (2), Zi Min (2), Ashton Nicholas (2), Galli Gina (2) (1) The University of Manchester , (2) The University of Manchester, Manchester, UK

Background/aims:
In vitro fertilization (IVF) is a highly effective fertility treatment that has led to the birth of over 10 million babies worldwide. While the procedure is generally safe, some studies suggest IVF can increase the risk of cardiovascular complications during pregnancy and beyond. This risk appears to be greater for women that have undergone frozen embryo transfer, verses fresh-embryo transfer. Hence, this study is particularly interested in the effects of in vitro fertilization on maternal cardiovascular outcomes

Methods:
The conditions for submission have been satisfied and the procedures were carried out in accordance with The Animals (Scientific Procedures) Act, 1986. Local ethical approval was granted by The University of Manchester Animal Welfare Ethical and Review Board. CD1 female mice (6 weeks old) were used for oocyte production; CD1 males (8 weeks) for sperm.
Embryos were cultured to the blastocyst stage and were either transferred immediately to a pseudo-pregnant mouse (fresh transfer) or frozen with vitrification and then transferred (frozen transfer).The control pregnancies were generated by mating CD1 female with male CD1 mice. The mice littered, and were weaned to 3 weeks and a cardiovascular assessment was then performed on the mothers using echocardiography.

Results:
Compared to controls, IVF increased interventricular septal thickness at end diastole, heart rate, left ventricular ejection fraction, left ventricular fractional shortening, aortic velocity and pulmonary velocity, and peak velocity of early diastolic mitral annular motion.
These results suggest IVF pregnancies can lead to exaggerated cardiac remodeling, which may predispose them to cardiovascular disease later in life.

Conclusions:
Mothers of IVF conceived pregnancies with fresh-embryo transfer and those with frozen-embryo transfer manifested a statistically significant increase in several cardiovascular structure parameters. Our findings indicate that IVF procedure may make a potential effect on cardiovascular structure and function, which calls for further investigation and longer-term follow-ups.

Funding:
Commonwealth Scholarship Commission

Key-words: (up to 5):
In vitro fertilization, Cardiovascular diseases, Cardiac remodeling, Infertility, Embryo transfer.

Abstract #00005047 en

Weight gain during key developmental periods and biological age acceleration in young adulthood: evidence from a Filipino cohort

Public Health Policies Across the Life Cycle.

Voloshchuk Romaniya (1), Mayol Nanette Lee (2), Carba Delia B (2), Adair Linda S (1) (1) University of North Carolina at Chapel Hill, (2) University of San Carlos, Talamban

Background/aims:
Epigenetic clocks use DNA methylation to estimate biological age acceleration (AgeAccel), capturing mortality and morbidity risk. Evidence has linked low birth weight and high adiposity in adolescence and adulthood with subsequent AgeAccel. We tested if gaining weight faster than expected, given one's growth trajectory is associated with AgeAccel at age 21yrs estimated by commonly-used epigenetic clocks and their combinations in a Filipino cohort.

Methods:
We used data from the Cebu Longitudinal Health and Nutrition Survey from 1983-2005 (n=1,745, 47% female). Relative weight gain (RWG) during key time intervals (0-6mo, 6mo-1yr, 1-2yrs, 2-8.5yrs, 8.5-11yrs, 11-15yrs, 15-18yrs, 18-21yrs) was represented by standardized residuals derived from regressing weight at the end of the given time interval on all previous weight and height (length if<2yrs) measurements, including at birth, and concurrent height. AgeAccel at 21yrs was estimated by six epigenetic clocks: HorvathAge, HannumAge, PhenoAge, GrimAge, DNA methylation estimator of telomere length (DNAmTL), and Dunedin Pace of Aging (DunedinPACE). Additionally, we created FactorAge using factor analysis of these clocks. We tested associations of RWG and AgeAccel using multivariate regression, adjusting for concurrent smoking, average lifetime wealth, immune cell proportions, and parity and total months breastfeeding in females . Analyses were sex-stratified and adjusted for multiple comparisons.
Sensitivity analyses tested if age of pubertal onset was a confounder.

Results:
We found one standard deviation (1SD) RWG 11-15yrs corresponded to 0.07(p<0.028) SD higher FactorAge in both sexes and 0.13(p=0.001) months/(year aged) faster DunedinPACE in females. 1SD RWG 18-21yrs correlated with 0.06(p=0.032) SD FactorAge and 0.12(p=0.002) months/(year aged) DunedinPACE in females. In males, RWG 1-2yrs corresponded to 4.47(p=0.005) months higher HorvathAge.

Conclusions:
Our results support the association of adolescent weight gain with AgeAccel, especially in females, regardless of pubertal timing. Male AgeAccel may be more sensitive to early-life weight gain, whereas adult weight gain may explain greater AgeAccel variation in females.

Funding:
Bill and Melinda Gates Foundation (OPP1164115), NIH/NHLBI 1T32HL129969 and NIH P2C HD050924 and R01AG061006

Key-words: (up to 5):

"epigenetic clock", longitudinal, "weight gain", sex-specific, "lower-middle-income country"

Abstract #00005051 en

Adverse Maternal Characteristics and Pregnancy Outcomes in Gestational Diabetes Highlights Need for Long-term Follow-up for Cardiometabolic Disease.

Big Data and Cohorts in DOHaD Research.

Kirkwood Jasmine (1), Manataki Areti (2), Wake Deborah (1), Lindsay Robert (3), Reynolds Rebecca (1) (1) University of Edinburgh, (2) University of St Andrews, (3) University of Glasgow

Background/aims:
Gestational diabetes mellitus (GDM) is a common complication that increases the risk of type 2 diabetes and early cardiovascular disease in both mother and child. Management includes lifestyle modification(L), metformin(M), or insulin(I). In Glasgow, UK, risk-based screening includes BMI of ≥35 kg/m2 and other factors, and World Health Organisation glucose thresholds. We hypothesised that GDM prevalence would be high and pregnancy outcomes similar to women without GDM

Methods:
We compared maternal characteristics of singleton pregnancy outcomes between women with (n=2137) and without GDM (n=22,930)(2021-2023, Glasgow, UK). We also compared outcomes by treatment:
L:[1245(58%)], M:[600(28%)], and I:[292(14%)]. Data are mean[SD] or N[%].

Results:
Women with GDM were older than non-GDM (32[5.3] vs 31[5.4] years, p<0.001), with the insulin group being the eldest (L:31[5.5], M:33[5], I:34[5]years, p<0.001). Non-GDM women BMI was overweight; GDM were obese, with the insulin group having the highest (GDM:33[7.4] vs non:27[5.7], p<0.001; L:32 [7.1], M:32[7.7], I:35[7.7]kg/m2, p<0.001). European ethnicity was most common across all groups (GDM:1,306[61%], non:17,483[76%]), but GDM had more African (GDM:189[9%],non:1068[5%]) and Southern-Asian (GDM:456[21%], non:1550[7%]). Caesarean births were higher with GDM compared to non-GDM (GDM:1159[54%] vs non:9461[41%], p<0.001), mostly elective (L:345[28%], M:202[34%], I:116[40%], p<0.001). There was no significant difference in the one-minute Apgar score (GDM vs non, p=0.218; L vs M vs I, p=0.633). Large for gestational age(LGA) infants were more common with GDM, especially with insulin (GDM:780[36%] vs non:5859[26%], p<0.001; L:427[34%], M:216[36%], I:137[47%], p<0.001). Neonatal intensive care unit(NICU) admissions were higher with GDM, with the highest in the insulin group (GDM:287[13%] vs non:1871[8%], p<0.001; L:157[13%], M:78[13%], I:52[18%], p=0.06)

Conclusions:
Prevalence of GDM was high at 9% despite only screening women with BMI≥35kg/m2. Women with GDM have higher age and BMI. GDM is associated with increased rates of caesarean births, LGA and NICU admissions, particularly with those requiring insulin. These mothers and children warrant lifelong follow-up for cardiometabolic disease

Funding:
Medical Research Scotland (PHD- 50224- 2020).

Key-words: (up to 5):
Pregnancy outcomes, Gestational Diabetes Mellitus, Complications,

Abstract #00005059 en

Renal NO-pathway impairment in neonatal rats treated with a dual endothelin receptor antagonist

Impact of Early Life Exposures and Environmental Pollutants

Oronel Lucas Humberto (1), Czernicyniek Analía (1), Magnanelli Ángeles (1), Marinoni Rocío (1), Martínez Carolina (1), Lores Arnaiz Silvia (1), Albertoni Borghese Florencia (1), Majowicz Mónica (1)
(1) Faculty of Pharmacy and Biochemistry (UBA)

Background/aims:
Previously, we demonstrated that inhibiting the endothelin (ET) system with a dual ET receptor antagonist (ERA) during the early postnatal period in rats decreased the number of glomeruli, this effect being more pronounced in males than in females. We also showed that these males increased systolic blood pressure following a high-sodium diet during adulthood.
Since the nitric oxide (NO) pathway plays a crucial role in renal development and an imbalance between NO/ROS is related to renal programming, we aimed to evaluate the NO pathway and NO/O2•- (superoxide) ratio in ERA-treated neonatal rats.

Methods:
Newborn SD rats were treated with a dual ERA (Bosentan 20 mg/Kg/day) or vehicle during their first 6 days of life. On day 7th, pups were sacrificed. Four experimental groups were studied: control males (CM), ERA-treated males (ERA-M), control females (CF), and ERA-treated females (ERA-F). We determined
NO/O2•- ratio and nNOS and eNOS mRNA expression by qPCR in renal homogenates. We also measured NADPH diaphorase activity on renal histological sections, analyzing different renal structures.
Statistics: 2-way ANOVA followed by Bonferroni post-test.

Results:
ERA-M and ERA-F had lower NO/O2•- ratio vs their respective control groups ($p<0.05$). NADPH-d activity decreased in glomeruli, immature structures, and macula densa cells of ERA-M vs CM ($p<0.05$), and decreased in immature structures and macula densa cells in ERA-F vs CF ($p<0.05$). Additionally, ERA-M had decreased nNOS and eNOS mRNA renal expression vs CM, while ERA-F had an increased nNOS and eNOS mRNA renal expression vs CF ($p<0.05$).

Conclusions:
The impaired NO pathway seen in ERA-treated neonatal rats could be playing a role in renal programming.
Females seem to be slightly more protected than males after ERA treatment.

Funding:
This work was supported by grants from the University of Buenos Aires (20020170100135BA). Protocol was approved by the Institutional Committee for Use and Care of Laboratory Animals from the School of Pharmacy and Biochemistry (REDEC-2024-3207-E-UBA-DCT_FFYB).

Key-words: (up to 5):
renal programming; endothelin inhibition; nitric oxide; neonatal rats

Abstract #00005119 en

The Evolving World of DOHaD: A Bibliometric Analysis

Public Health Policies Across the Life Cycle.

Oewel Thais de Souza (1), Blumrich Lukas (1), Ferraro Alexandre Archanjo (2)
(1) Faculty of Medicine of the University of São Paulo, (2) Department of Pediatrics, Faculty of Medicine of the University of São Paulo

Background/aims:
The field of Developmental Origins of Health and Disease (DOHaD) has grown substantially since its inception, with increasing focus on global, especially developing, contexts. However, a comprehensive mapping of its scientific landscape is still lacking. This study aimed to explore the evolution of DOHaD research through bibliometric analysis and to assess its intersection with the One Health paradigm.

Methods:
We conducted a bibliometric analysis using the Web of Science Core Collection, targeting DOHaD-related keywords in titles, abstracts, and author keywords, based on MeSH terms, using VOSviewer and the Bibliometrix package in R. We analyzed both DOHaD literature and its citing publications, and searched for thematic overlap with One Health literature. As this study involved secondary analysis of published literature, no human or animal subjects were involved.

Results:
A total of 6,085 journal articles were identified from 1962 to 2025, accruing 155,207 citations. Among these, 4,169 were original articles and 1,396 were reviews. The most common publication categories were Public, Environmental and Occupational Health (10.6%), Endocrinology/Metabolism (9.7%), Nutrition/Dietetics (9.0%), Biochemistry (7.0%), and Neurosciences (6.7%). The leading publishing countries were the USA, UK and Canada. Collaboration networks between countries revealed strong research partnerships primarily among high-income nations. Analysis of temporal keyword trends revealed five dominant research clusters. Citing literature primarily stemmed from Neurosciences, Biochemistry and Endocrinology. Only three articles demonstrated explicit overlap with the One Health domain.

Conclusions:
DOHaD research has experienced linear growth, with a slight decline in the past two years. The field remains concentrated in developed nations, highlighting the need for more equitable global collaboration. Since 2010, “epigenetics” has emerged as the dominant keyword, reflecting the field’s mechanistic turn. The prevalence of open-access publications supports broader accessibility. Although conceptually aligned, practical intersections between DOHaD and One Health remain limited and warrant further integration.

Funding:
FAPESP (Fundação de Amparo à Pesquisa do Estado de São Paulo)

Key-words: (up to 5):
metascience, review, bibliometrics, public health, one health

Abstract #00005131 en

Sampling across socioeconomic strata: A geographic strategy for pregnancy cohort recruitment in intergenerational studies

Big Data and Cohorts in DOHaD Research.

Serrano-Lomelin Jesus (1), Wowdzia Jenna (2), Van Lieshout Ryan J. (3), Sycuro Laura (4), Kozyrskyj Anita (5), Giesbrecht Gerald (4), Hicks Matthew (5), Jain Venu (5), Krzeczkowski John E. (6), Pei Jacqueline (5), Walter Jens (7),
Ospina Maria B. (8)
(1) Department of Public Health Sciences / Queen's University, (2) Women and Children's Health Research Institute, (3) McMaster University, (4) University of Calgary, (5) University of Alberta, (6) Brock University, (7) University College Cork, (8) Queen's University

Background/aims:
The Society, Pregnancy, Postpartum & Infant Development (SPPIN) project investigates whether gut microbiota mediates the relationship between social influences, perinatal mental health and child neurodevelopment. A key challenge is recruiting a socioeconomically diverse cohort of pregnant people, since traditional probabilistic sampling methods are often inefficient for capturing variation across socioeconomic strata. We aimed to develop a geographic sampling framework based on area-level socioeconomic deprivation to enhance representativeness.

Methods:
The SPPIN pregnancy cohort is based in Edmonton, Canada. Sample size was estimated using a longitudinal study design and anticipated effect sizes for mediation pathways. The Canadian Pampalon Material and Social Deprivation Index was used to rank and map geographic areas into quintiles of deprivation (Q1 = least deprived, Q5 = most deprived) using 2021 Canadian census data. The proportion of participants of reproductive age in each quintile informed proportional allocation of the sample. Recruitment efforts are guided by monthly mapping of residential postal codes by deprivation level to monitor sampling targets are met by area.

Results:
The planned sample size is 600 pregnant people. A total of 1,272 geographic areas were classified into socioeconomic deprivation quintiles. Target sample allocation by quintile was: Q1 (20.4%), Q2 (19.7%), Q3 (18%), Q4 (22.8%), and Q5 (19.1%). After four months of recruitment, 62 participants have been enrolled: Q1 (37%), Q2 (24.2%), Q3 (16.1%), Q4 (8.1%), and Q5 (9.7%). Recruitment to date has overrepresented participants from less deprived areas, highlighting the need to strengthen efforts in the most deprived areas (Q4-Q5) moving forward.

Conclusions:
Using geographic information systems and area-level deprivation indices can support more equitable and representative sampling in pregnancy cohorts. Targeted strategies are needed to improve recruitment in highly deprived areas to ensure findings reflect the diversity of social contexts.

Funding:
Canadian Institutes of Health Research (#487536) and Canada Research Chairs Program (CRC-2023-00153).

Key-words: (up to 5):
Gut Microbiota, Perinatal Mental Health, Infant Development, Cohort Profile on Social Location

Abstract #00005149 en

Neurodevelopmental Impacts of a Perinatal High-Fat Diet: Pups Milestones, Neonatal Murinometry, and Maternal Behavior and Biomarkers

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Lazzaretti Camilla (1), Vieira Carletti Jaqueline (2), Barbosa Gonçalves Ariel (1), Ângelo Smaniotto Thiago (1), Daroda Dutra Francisco (1), Alves Joelma (1), Mesquita Peres Ariadni (1), da Silva Santos Eduardo (1), Lise Tusset Bruna (1), Guisolfo Machado Brenda (1), Nicola Fülber Isabella (1), César Burtzlaff Nadine (1), Tessari Lopes de Oliveira Giovana (1), Dalmaz Carla (1)
(1) Universidade Federal do Rio Grande do Sul (UFRGS), (2) Hospital de Clínicas de Porto Alegre

Background/aims:
Maternal consumption of a high-fat diet (HFD) during the perinatal period may alter glucose and circulating fatty acid levels, compromising offspring development, including delays achieving in motor and cognitive milestones in both rats and humans. It may also affect maternal behavior. This study aimed to evaluate the effects of a HFD on developmental milestones, neonatal murinometric parameters, maternal behavior, and biochemical markers in rats.

Methods:
Nulliparous female rats (90 days-old) were divided into two groups: HFD (N=6) and Standard Diet (SD, N=6). Diet was provided from gestational day 0 until weaning. The study included two cohorts of animals: (i) first, a cesarean section was performed on gestational day 19.5 to measure the weight and craniocaudal length of the neonates, as well as maternal blood glucose and ketones; (ii) second, offspring developmental milestones were assessed on postnatal days 6, 8, 10, 13, and 16, evaluating locomotion, cliff aversion, negative geotaxis and righting reflexes, and maternal behavior was analyzed (Pups: HFD, N=15; SD, N=15). Repeated-measures ANOVA were performed. Ethics Committee (UFRGS, #43424).

Results:
Offspring from the HFD group exhibited delayed locomotion ($P=0.042$), and accelerated response in negative geotaxis ($P=0,040$). No differences were observed in cliff aversion, or righting reflex tests ($P>0.05$). Maternal behavior was not impaired ($P>0.05$). The weight and craniocaudal length of the neonates were lower in the HFD group compared to the SD group ($P<0.001$). Maternal ketone levels were elevated ($P=0.032$), whereas blood glucose levels did not show significant differences ($P>0.05$).

Conclusions:
A HFD may contribute to reduced fetal growth, suggestive of impaired uteroplacental circulation, and motor delays in locomotion during offspring development. These findings are preliminary, and additional studies are needed to confirm these observations.

Funding:
Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS).

Key-words: (up to 5):
Maternal obesity; Maternal Behavior; Neurodevelopmental milestones; Locomotion.

Abstract #00005151 en

Impaired placental and fetal microcirculation in a mouse model of preeclampsia

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Fernandes-Santos Caroline (1), Leal Lamarca Bomfim Daniella (2), das Índias dos Santos Carvalho Fábio (2), Nunes G. S. Pereira Evelyn (2), Rangel Silvares Raquel (2), Lino Rodrigues Karine (2), Peres de Araújo Beatriz (2), Mello de Souza Elen (2), Daliry Anissa (2)
(1) Universidade Federal Fluminense, (2) Oswaldo Cruz Foundation

Background/aims:
Preeclampsia (PE) is a hypertensive disorder that develops after the 20th week of gestation and is characterized by complications such as proteinuria and multiorgan dysfunction due to systemic inflammation and endothelial dysfunction. Thus, we investigated the fetoplacental microcirculation in a PE model in mice using laser speckle fluxometry (LSF).

Methods:
Ethical approval L-016/2021. PE was induced from gestational day (GD) 11.5 to 18.5 by L-NAME 50 mg/Kg/day. We assessed the mother's systolic blood pressure (SBP), proteinuria, fetus biometry, and fetus and placental microcirculation. Data are expressed as mean ± SEM, analyzed by Student's t-test, $p<0.05$, n=10/group.

Results:
PE mothers had increased SBP (227.7±10.5 vs. CTL: 150.4±3.4 mmHg; $p<0.0001$) and proteinuria (88.3±11.4 vs. CTL: 15.11±6.5 mg/dL; $p=0.0001$) at GD17.5 compared to control group. The PE group had a decreased number of fetuses/mothers (6.67±0.41 vs. CTL: 8.2±0.29; $p=0.011$) and an increased number of placenta resorption sites (1.7±0.2 vs. CTL: 0.9±0.21; $p=0.024$). In fetus biometry, we observed a reduced elbow-paw length (0.36±0.009 vs. CTL: 0.39±0.007 cm; $p=0.04$) and foot length (0.26±0.005 vs. CTL: 0.29±0.006 centimeters; $p=0.004$). Finally, fetus from PE mothers had decreased flowmetry in the placenta (54.28±5.4 vs. CTL: 78.64±3.9 APUs; $p=0.0109$), umbilical cord (43.6±5.2 vs. CTL: 75.21±7.1 APUs; $p=0.0011$), thorax (92.0±7.0 vs. CTL: 126.9±7.9 APUs; $p=0.0027$), kidney (79.4±4.4 vs. CTL: 105.2±9.6 APUs; $p=0.0093$), paw (40.0±2.2 vs. CTL: 55.9±3.9 APUs; $p=0.0007$), transverse sinus (96.2±4.8 vs. CTL: 124.3±8.2 APUs; $p=0.0080$), anterior facial vein (101.0±7.2 vs. CTL: 129.8±8.4 APUs; $p=0.0236$), and cephalic vein (82.5±6.3 vs. CTL: 108.1±6.5 APUs; $p=0.0083$).

Conclusions:
L-NAME-induced PE was associated with impaired fetoplacental and fetal microcirculation, as shown by reduced blood flow in multiple anatomical regions. These findings highlight the relevance of this model for studying PE pathophysiology and its impact on fetal development, allowing the search for new treatments with potential impact on maternal and child health.

Funding:
CAPES, FAPERJ, CNPq e FIOCRUZ

Key-words: (up to 5):
Preeclampsia. Placenta. Microcirculation. Fetus. L-NAME.

Abstract #00005153 en

Silent pollution at the beginning of life: first steps of the PA-MAMI cohort

Impact of Early Life Exposures and Environmental Pollutants

Castillero-Rosales Irene (1), Barría-Almengor Felipe (2), Olea Nicolás (3), Iribarne-Durán Luz (4)
(1) Departamento de Química Analítica, Universidad de Panama, Panamá, (2) Departamento de Química Analítica, Universidad de Panamá. Panamá, (3) Departamento de Radiología y Medicina Física. Universidad de Granada. España, (4) Centro Nacional de Sanidad Ambiental, Instituto de Salud Carlos III

Background/aims:
In Latin America, particularly in rural regions such as Panama's Azuero Peninsula, understanding the impact of environmental pollutants on health requires integrative and contextualized approaches. The PA-MAMI maternal-child cohort, established in 2017, investigates exposure to endocrine-disrupting compounds (EDCs) through biomonitoring of biological matrices like placenta and breast milk. This approach aims to characterize the chemical exposome during critical developmental stages, identify potential sources of exposure, and generate evidence to inform preventive public health policies.

Methods:
The study recruited 60 pregnant women in their third trimester (Bioethics approval CBIUP 2016-MV-01-003). Participants completed questionnaires on sociodemographic, behavioral, and environmental factors. Concentrations of 32 endocrine disruptors were analyzed in placenta and breast milk using gas chromatography-tandem mass spectrometry (GC-MS/MS) and ultra-high-performance liquid chromatography (UPLC–Xevo TQ-XS). The estrogenic activity of placental extracts was evaluated using an e-screen assay on MCF-7 breast cancer cells. Data was analyzed using linear and logistic regression models to explore associations and exposure patterns.

Results:
Persistent organic pollutants (ΣPOPs 1.25 ng/mL) were found in all placental samples, despite their banned use decades ago, highlighting their environmental persistence. Breast milk samples showed widespread presence of bisphenols, parabens, benzophenones (ΣPlasticizers 29.63 ng/mL), and perfluoroalkyl substances (ΣPFAS 1088 ng/mL). All placental extracts exhibited estrogenic activity (mean TEXBα: 1.24 Eeq pM/mL).

Conclusions:
Ongoing biomonitoring of the maternal-child population is essential to evaluate control measures for environmental pollutants and to understand cumulative exposure during sensitive developmental windows such as pregnancy and early infancy. This study underscores the urgent need for comprehensive, evidence-based preventive strategies to support safe breastfeeding, minimize toxic exposure, and reduce long-term health risks across the life course. To our knowledge, this is the first biomonitoring effort in Panama in over 35 years, providing a critical baseline. A follow-up study is underway to assess longitudinal exposure trends and related health outcomes in the PA-MAMI cohort.

Funding:
Horizon Europe program (Grant N◦. 101057014, PARC), SENACYT-Panama (APY–NI–2015-05 and MOV-2023-12), National Audubon Society through a grant by Interamerican Development Bank (IDB) and the UK Blue Carbon Fund, and the Spanish

Ministry of Health (PI16/01820, PI17/01743, PI23/01389 and PI23/01884) and Consortium for Research in Epidemiology and Public Health (CIBERESP).

Key-words: (up to 5):
Panamá, Novel Entitities, Endocrine disruptors, PA-MAMI, Public Health

Abstract #00005155 en

The Epigenesis of an Egalitarian Society: Impact on caesarian section

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Kempe Annica (1) (1)
Karolinska Institutet

Background/aims:
Cesarean section (CS) delivery has substantially increased globally over the past few decades, reaching almost 30 million in 2020. This escalating trend has been observed in all regions and has emerged as a critical global health concern. This study addresses the practice of CS as an intrinsic part of culture. I examine the prevalence of CS among populations in the world with a matrilineal cultural heritage.

Methods:
A step-wise interdisciplinary research approach was used: 1) The conduct of a literature review to identify matrilineal societies globally, including the now existing as those of the past 2) Study of the epidemiology of CS for the specific geographical areas 3) Search through sources in anthropology, archaeology, history and art to obtain knowledge about the social norms inherent in matrilineal society.

Results:
Matrilineal societies were found in Asia, Africa, Europe, Oceania and the Americas. Some were found in indigenous contexts. Regardless of whether matrilineal culture was practiced or fully practiced today, the prevalence of CS was consistently lower for any population with a matrilineal cultural heritage. Where current epidemiological research was unable to explain differences in the prevalence of CS within similar populations, historical maps were cross-matched to the geography of present-day country boundaries showing the presence of past matrilineal culture: The status of women historically was different in the locations with lower CS prevalence today.

Conclusions:
The practice of CS is deeply rooted in culture and the status of women. The egalitarian status of women and men characteristic of matrilineal society and documented lesser violence against women are plausible explanations. How women's high status in existing and formerly existing matrilineal societies seems to create resiliency to reproductive anxiety and CS practice needs attention.

I certify that the conditions for submission have been satisfied and that all animal and human welfare and ethical considerations have been met.

Funding:
Karolinska Institutet, Swedish Society for Psychosocial Obstetrics and Gynecology

Key-words: (up to 5):
Caesarian section; Violence against women; Egalitarian; Matrilineal; Indigenous

Abstract #00005157 en

Umbilical endothelium-derived thrombospondin-1 (TSP-1) of preeclampsia decreases the angiogenic capacity of brain endothelial cells

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Escudero Esthefanny (1), Acurio Jessenia (2), D Mistry Hiten (3), Kurlak Lesia (4), Moore-Carrasco Rodrigo (5),
Escudero Carlos (6)
(1) Faculty of Health Sciences, University of Talca, Talca, Chile, (2) Vascular Physiology Laboratory, Universidad del Bío-Bío, Chillán, Chile, (3) Division of Women and Children's Health, King's College London, United Kingdom (H.D.M.).,
(4) Stroke Trials Unit, School of Medicine, University of Nottingham, United Kingdom , (5) Faculty of Health Sciences, University of Talca, Talca-Chile, (6) Vascular Physiology Laboratory, Universidad del Bío-Bío, Chillán, Chile.

Background/aims:
Placental dysfunction in preeclampsia (PE) has been associated with altered neurodevelopment. Since the placental vasculature is continuous with fetal circulation, placental-derived circulating factors may reach the fetal brain and impair angiogenesis. Previous studies have shown reduced cerebral angiogenesis in offspring from preeclamptic pregnancies. Thrombospondin-1 (TSP-1), an antiangiogenic glycoprotein, is elevated in PE placentas, but its role in the placenta-brain communication axis remains unexplored. To analyze the effect of secreted factors from umbilical endothelial cells, particularly TSP-1, on the angiogenic and invasive capacity of cerebral endothelial cells using an in vitro model.

Methods:
Primary human umbilical vein endothelial cells (HUVECs) from normal pregnancies (NP, n=6) and PE (n=6) were used to obtain conditioned media (CM-HUVEC-NP, CM-HUVEC-PE), which were applied to human cerebral microvascular endothelial cells (hCMEC/D3). Tube formation, migration, invasion, and actin cytoskeleton remodeling were assessed, along with the expression of angiogenic markers. Proteomic analysis was also performed on umbilical cord plasma from NP and PE pregnancies (n=3 per group).

Results:
Results showed that MC-HUVEC-PE significantly impaired tube formation, migration, and invasion of hCMEC/D3 cells ($p<0.03$), accompanied by cytoskeletal remodeling abnormalities, such as longer but fewer actin fibers and the formation of filopodia. Proteomic profiling revealed 30 differentially expressed proteins in PE umbilical cord plasma, including a significant increase in TSP-1, which was confirmed by Western blot. TSP-1 was also ~3-fold elevated in MC-HUVEC-PE compared to MC-HUVEC-NP ($p<0.03$). Importantly, the antiangiogenic effects of MC-HUVEC-PE were reversed by a neutralizing anti-TSP-1 antibody.

Conclusions:
TSP-1 secreted by umbilical endothelial cells in PE may contribute to reduced cerebral angiogenesis, providing novel evidence of a placenta-brain communication pathway impacting fetal neurovascular development.

Funding:
Fondecyt Regular 1240295

Key-words: (up to 5):

Preeclampsia, Thrombospondin 1, angiogenesis, placenta-brain communication, secretome.

Abstract #00005275 en

Human milk oligosaccharide composition and association with maternal factors in the GUSTO multi-ethnic Asian population

Role of Infant and Young Child Feeding Practices on Long-Term Health

Zhang Han (1), Ang Li Ting (1), Pang Wei Wei (2), Wee Charlene (1), Wong Chun Hong (1), Spann Kennedy (3), Chua Mei Chien (4), Yap Fabian (4), Tan Kok Hian (4), Chong Yap Seng (2), Karnani Neerja (5), Mueller-Riemenschneider Falk (6), Natarajan Padmapriya (2), Godfrey Keith (7), Gluckman Peter (8), Eriksson Johan (1), Geddes Donna (9), Wlodek Mary E (10), Bode Lars (3), Chan Shiao-Yng (2)
(1) Institute for Human Development and Potential (IHDP), A*STAR, Singapore, (2) Yong Loo Lin School of Medicine, National University of Singapore, Singapore, (3) Department of Pediatrics and the Human Milk Institute (HMI), University of California San Diego, USA, (4) Duke-NUS Medical School and KK Women's and Children's Hospital, Singapore, (5) Bioinformatics Institute, Agency for Science, Technology and Research (A*STAR), Singapore, (6) Saw
Swee Hock School of Public Health, National University of Singapore, Singapore, (7) University of Southampton and University Hospital Southampton NHS Foundation Trust, United Kingdom, (8) Liggins Institute, University of Auckland,
New Zealand, (9) School of Molecular Sciences, The University of Western Australia, Australia, (10) Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Australia

Background/aims:
Human milk oligosaccharides (HMOs) are bioactive components of human milk that influence infant development. Their composition is shaped by genetic and environmental factors, but studies in Asian populations remain sparse, limiting development of HMO strategies to promote Asian infant health. This study aimed to investigate the HMO composition, longitudinal changes and the influence of maternal factors in a multi-ethnic Asian cohort.

Methods:
In this prospective GUSTO mother-offspring cohort study, maternal sociodemographic, genetic, and obstetric characteristics, were associated with the 19 most-abundant HMOs (quantified by HPLC) in human milk collected from 248 mothers at 3-weeks (n=205) and 3-months (n=114) postpartum (71 matched cases, 28.6%).

Results:
Mothers were predominantly Chinese (73.8%), followed by Malay (14.5%) and Indian (11.7%). Across ethnicities, individual HMO concentrations and proportions of secretors, were comparable. Approximately
70% were secretors, determined by distinctly higher 2'-fucosyllactose (2'-FL, 3-weeks: mean±SEM 2391±137nmol/mL, 16.0% of total HMO; 3-months: 1677±114nmol/mL, 10.4%) and lacto-N-fucopentaose-I (LNFP-I) compared with non-secretors (2'-FL, 3-weeks: 29±5nmol/mL, 0.3%; 3-months: 28±4nmol/mL, 0.2%). 3-fucosyllactose (3-FL) comprised 9.5% and 21.7% of the total HMO concentration in secretors and non-secretors respectively at 3-weeks, and 30.4% and 42.9% respectively at 3-months. Compared to term, preterm delivery associated with higher 3'-sialyllactose (3'-SL) at 3-weeks [adjusted mean difference 1.23SDs (95%CI 0.44, 2.01); p=0.002]. Longitudinally, there were consistent changes in individual HMO concentrations from 3-weeks to 3-months in both secretor groups. HMO secretor-phenotype showed 97% concordance with status predicted by the FUT2 single nucleotide polymorphism (SNP) rs1047781.

Conclusions:

The three major Asian ethnicities displayed similar HMO composition, with the FUT2 rs1047781 SNP being a key determinant of secretor status. Preterm delivery may influence early postpartum HMO composition, increasing particularly the 3'-SL concentration. Concentrations of 2'FL were lower, while 3-FL higher, compared with published reports on non-Asians, suggesting multi-ethnic studies of infant nutrition and health require consideration of Asian HMO biology.

Funding:
Singapore National Research Foundation under its Human Potential Program (H23P1M0004)

Key-words: (up to 5):
human milk oligosaccharides, secretor status, Asian ethnicity, maternal factor, FUT2 gene

Abstract #00005290 en

Intrauterine Growth Restriction affects adipose tissue morphology, lipid metabolism and inflammatory profile throughout postnatal life in pigs

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Pires Dayanne Kelly Oliveira (1), Dominique Fernandes Saffir (1), Lopes-Ferreira João Vitor (1), Riverosa José Andrés Nivia (1), Alkmim Tulio Cezar Caiafa de (1), Almeida Fernanda Radicchi Campos Lobato de (1) (1) Universidade Federal de Minas Gerais - UFMG

Background/aims:
Intrauterine Growth Restriction (IUGR) affects around 10% of human births and is associated with an increased risk of metabolic and inflammatory disorders throughout life. In pigs, this condition occurs naturally, because of placental insufficiency. Due to the anatomical, physiological and metabolic similarities to humans, pigs are a suitable translational model for studies on fetal programming. This study aimed to evaluate IUGR effects on adipose tissue morphology, lipid metabolism and inflammatory profile throughout postnatal development.

Methods:
Littermate male piglets were selected at birth, according to birthweight, and allocated in: IUGR (0.7-1.0 kg; n=120) or normal birthweight (NW, 1.6-1.9 kg; n=120). Animals were monitored until 150 days, and euthanasia performed at birth, 26, 70 and 150 days. Biometrical, biochemical and histomorphometrical analyses of adipose tissue and quantification of plasma cytokines (IL-6, IL-8, IL-10, IL-12p70, TNF, IL-1β) were carried out (CEUA/UFMG nº 2016/342). Variables were analyzed using SAS general linear models (GLM) with multiple comparisons (Tukey-Kramer) and correlations (Pearson/Spearman), considering $P<0.05$ as significant.

Results:
RIUC animals showed lower body weight, body mass index at all ages and significant changes in total cholesterol, LDL and Castelli I index levels($P<0.05$). There was a higher density and predominance of small adipocytes in the visceral adipose tissue at 150 days. RIUC pigs showed increased IL-6 and IL-12 levels at 70 days, with positive correlations between larger adipocytes and pro-inflammatory cytokines (IL-6, IL-8 and TNF-α)($r = 0.96$, $P = 0.013$), indicating deregulation and a potentially harmful profile, given the negative impact of these cytokines on systemic levels when exacerbated.

Conclusions:
IUGR promotes long lasting changes in post-natal growth, metabolism and the immune system, showing an increased risk of chronic metabolic disorders. These results reinforce the importance of fetal programming in the development of metabolic diseases with public health implications.

Funding:
CNPq e CAPES.

Key-words: (up to 5):
RIUC; lipid metabolism; adipocytes; cytokines; fetal programming.

Abstract #00005326 en

Maternal weight gain during pregnancy is sex-specifically linked to intrauterine growth restriction in the offspring of obese rats

Mechanisms Determining Transgenerational Effects of Health and Disease

Ibáñez-Chávez Carlos Alberto (1), Vargas-Hernández Lilia (2), Reyes-Castro Luis Antonio (3), Rodríguez-González Guadalupe Leticia (3), Juárez-Pilares Gimena (4), Zambrano-González Elena (1)
(1) Biol Reproducción, Instituto Nacional de Ciencias Médicas y Nutrición SZ/Facultad de Química, UNAM, (2) Biol Reprod, Ins Nal de Ciencias Médicas y Nutrición SZ/Hosp GinecObst #4 Luis Castelazo Ayala, IMSS, (3) Departamento de Biología de la Reproducción, Instituto Nacional de Ciencias Médicas y Nutrición SZ, (4) Depto Investigación Experimental y Bioterio, Instituto Nacional de Ciencias Médicas y Nutrición SZ

Background/aims:
Maternal gestational weight gain (GWG) may be related to altered placental function and Intrauterine Growth Restriction (IUGR). Maternal obesity (MO) increases small for gestational age (SGA) fetuses in rodents. The links between GWG and fetal-placental outcomes remain unclear. We aimed to assess GWG in relation to fetal and placental size by sex in MO.

Methods:
Female Wistar rats were weaned onto chow (C, n=8) or a high-fat diet (MO, n=12) and mated at 120 days. Daily GWG was modeled by cubic regression. At gestational day 19 (GD19), % of small/low (<5th C percentile) fetal weight (FW), placental weight (PW), and placental efficiency (PE=log[FW/PW]) was determined by sex in group-pooled litters (11–17 fetuses/litter). GWG rate (cubic model derivative) at GD19 was associated with FW, PW, and PE by linear regression. Data are Mean±SEM; $p<0.05$ by t-test or chi-squared test. All procedures followed institutional ethical guidelines.

Results:
Daily GWG strongly fit a cubic function (C:R=0.995; MO:R=0.996). Maternal weight was higher in MO vs. C at mating (404±9 vs. 312±5g), but lower GWG (96±5 vs. 120±5g) and GWG rate (13±1 vs. 19±1g/d) were observed in MO vs. C at GD19. SGA was elevated in MO males (83%) and females (57%), while low PW (15%) and PE (25%) were increased in MO males only. GWG rate showed moderate positive correlation with FW (males:R=0.593; females:R=0.512), weak positive correlation with PE (males:R=0.307; females:R=0.289), and no correlation with PW.

Conclusions:
The GWG trajectory exhibits early gain, mid slowdown, and late acceleration, described by a cubic function. This model may serve as a simple, non-invasive tool to assess fetal development during gestation. Reduced GWG rate in MO at late gestation is associated with IUGR and sex-specific effects on placental size and efficiency.

Funding:
Newton Fund RCUK-CONACyT FONCICYT/49/2016.

Key-words: (up to 5):
Small for gestational age, Placental function, Fetal weight, Placental efficiency, Gestational weight gain rate

Abstract #00005332 en

Growth trajectories of maternal obesity prior to pregnancy are associated with intrauterine growth restriction in rats

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Vargas-Hernández Lilia (1), Ibáñez-Chávez Carlos Alberto (2), Reyes-Castro Luis Antonio (3), Rodríguez-González Guadalupe Leticia (3), Juárez-Pilares Gimena (4), Zambrano-González Elena (2)
(1) Biol Reprod, Ins Nal de Ciencias Médicas y Nutrición SZ/Hosp GinecObst #4 Luis Castelazo Ayala, IMSS, (2) Biol Reproducción, Instituto Nacional de Ciencias Médicas y Nutrición SZ/Facultad de Química, UNAM, (3) Departamento de Biología de la Reproducción, Instituto Nacional de Ciencias Médicas y Nutrición SZ, (4) Depto Investigación Experimental y Bioterio, Instituto Nacional de Ciencias Médicas y Nutrición SZ

Background/aims:
Maternal obesity (MO) is often associated with offspring intrauterine growth restriction (IUGR) in animal models. However, the relationship between maternal body weight (BW) and IUGR remains poorly understood. The rat growth curve can be modeled by the Gompertz function, with parameters for maximal BW (<a>), growth rate near the inflection point (<b>), and its timing (<x_o>). We aimed to examine whether fetal weight (FW) could be predicted from pregestational MO growth trajectories.

Methods:
Female Wistar rats (F0) were weaned at 21 days of age (d) onto Chow (C, n=8) or a High-Fat Diet (HFD) in MO (n=12), weighed weekly and mated at 120 d with non-experimental males. Pregnant F0 and fetuses were euthanized for sex and FW recording at 19 days of gestation. Pregestational BW were fit to Gompertz function by nonlinear regression, and <a> and <b> parameters were tested as predictors of male and female FW using multiple linear regression. Data are shown as mean ± SEM, $p<0.05$. Statistical comparisons: F0 parameters by t-test and FW by 2W-ANOVA. All procedures followed institutional ethical guidelines.

Results:
Gompertz parameters were increased in MO vs. C (<a>: 427±10 vs. 316±6 g), (<b>: 28±1 vs. 19.3±0.3 d^{-1}), and (<x_o>: 42±1 vs. 32±1 d,). FW was lower in MO vs. C for both males (2.17±0.33 vs. 2.79±0.79 g) and females (2.16±0.52 vs. 2.66±0.66 g), and was predicted by <a> in males but not in females, while <b> predicted FW in both sexes (R=0.7).

Conclusions:
Maternal obesity increased the maximal maternal BW and growth rate around a delayed inflection point <x_o> respect to C. Gompertz parameter <a> indicated sexual dimorphism in fetal development linked to maternal pregestational growth. Parameter <b> was a sex-independent FW predictor, supporting its role as an IUGR biomarker.

Funding:
Newton Fund RCUK-CONACyT FONCICYT/49/2016.

Key-words: (up to 5):
Pregestational growth trajectories, Gompertz function, Fetal weight, Growth parameters, IUGR biomarker

Abstract #00005334 en

Preconception Paternal Exposure to PFAS Mixtures Modifies Sperm Methylation and Offspring Transcriptome, Driving Sexually Dimorphic Cardiometabolic Outcomes in Mice

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Pilsner Richard (1), Maxwell DruAnne (1), Paskavitz Amanda (1), Houle Emily (1), Roth Katherine (1), Gurdziel Katherine (1), Petriello Michael (1)
(1) Wayne State University

Background/aims:
Perfluoroalkyl and polyfluoroalkyl substances (PFAS) are diverse synthetic chemicals with long half-lives and are widespread environmental contaminants. Emerging data suggest that PFAS exposure affects male reproductive health; however, the precise mechanisms and intergenerational effects remain unclear. Therefore, our study aimed to examine the impact of male PFAS exposure on sperm DNA methylation and gene expression in the offspring's placenta and liver.

Methods:
Adult 9-week-old C57BL/6J male mice were exposed to five PFAS substances (~0.32 mg/kg/day) for eight weeks or to a vehicle control through their drinking water and were then mated with unexposed females prior to sacrifice. Reduced representation bisulfite sequencing (RRBS) was performed on epididymal sperm, and bulk RNA sequencing (RNA-seq) was conducted using the NovaSeq platform on embryonic day 12.5 (E12.5) placenta and 8-week-old offspring liver. Gene ontology analysis for significant changes in methylation and gene expression was performed using Metascape. The animal protocol was approved by the Wayne State University Institutional Animal Care and Use Committee.

Results:
PFAS exposure resulted in 2861 differentially methylated regions (DMRs; $q<0.05$) in sperm. Gene ontology of sperm DMRs revealed enrichment in multiple developmental processes, including lung epithelial cell differentiation and morphogenesis. Compared to controls, male offspring sired by PFAS-exposed fathers exhibited 71 differentially expressed genes (DEGs; $p<0.05$) in the E12.5 placenta, which were enriched in developmental pathways, and 40 DEGs in 8-week-old livers, enriched in cholesterol metabolic processes and responses to xenobiotic stimuli. Additionally, livers of male offspring from PFAS-exposed fathers displayed higher cholesterol levels ($p<0.05$). No cholesterol-related effects were observed in female offspring.

Conclusions:
Our results demonstrate that paternal preconception PFAS exposure leads to aberrant sperm methylation and subsequent sexually dimorphic health effects in F1 offspring, potentially mediated through placental programming. These novel findings suggest that male preconception PFAS exposure influences the long-term programming of offspring gene expression in a sex-specific manner.

Funding:
National Institute of Health P30ES020957

Key-words: (up to 5):

Paternal, Preconception, sperm, placenta, metabolism.

Abstract #00005336 en

Mouse nephron formation is impaired by moderate dose arsenical exposure

Impact of Early Life Exposures and Environmental Pollutants

Alonso Carlos Agustin Isidro (1), Haverfield Jenna (2), Regalado Gabriela (3), Sellami Sihem (4), Gagnon Natascha (5), Rajaram Ajay (6), Fiset Pierre-Olivier (6), Ryan Aimee K (4), Mann Korren K (5), Gupta Indra R (7)
(1) McGill University Health Centre, (2) The Research InstituteMcGill University Health Center, (3) McGill University Health Center, (4) The Research Institute of the McGill University Health Centre, (5) Lady Davis Institute for Medical Research, Jewish General Hospital, McGill University, (6) Department of Pathology, McGill University, (7) The Research Institute of the McGill University Health Centr

Background/aims:
Millions of people are exposed to concentrations of arsenic that exceed the World Health Organization's limit of 10 µg/L. Inorganic arsenic (iAsIII) is metabolized by arsenic 3 methyltransferase (As3mt) that converts it to methylated arsenicals, mono and dimethyl arsonous acid (MMA and DMA). Chronic arsenic exposure is linked to an increased risk of chronic kidney disease, however, the effects of arsenic on kidney development remain unclear. We hypothesized that exposure to arsenicals impairs ureteric bud brunching during mouse kidney development.

Methods:
Ex vivo: Dams carrying a Hoxb7-GFP allele were sacrificed at pregnancy day 11 (E11.5) or 12 (E12.5) or 13 (E13.5). Embryonic kidneys of Hoxb7-GFP+ embryos were dissected and cultured in the presence or absence of 200 µg/L sodium arsenite (iAsIII), MMAIII, MMAV and DMAV. Fluorescent and brightfield images were taken at 0 and 48 h of culture to quantify branching and explant size.
In vivo: Humanized AS3MT pregnant mice (in which the mouse As3mt locus is replaced with the human AS3MT locus to model human arsenic metabolism) were administered tap water or water supplemented with 200 µg/L of iAsIII throughout gestation. Pups were euthanized on postnatal day 15, and the kidneys were weighed and total nephron number quantified.

Results:
In vivo: Humanized AS3MT pregnant mice (in which the mouse As3mt locus is replaced with the human AS3MT locus to model human arsenic metabolism) were administered tap water or water supplemented with 200 µg/L of iAsIII throughout gestation. Pups were euthanized on postnatal day 15, and the kidneys were weighed and total nephron number quantified.

Conclusions:
Conclusions: Exposure to arsenicals during mouse embryonic development impairs ureteric bud branching morphogenesis and decreases nephron endowment.

Funding:
Funding: This project is part of the DERIVE (DEvelopmental Research on Interactions between Variants and the Environment) research program and is funded by an anonymous donor through the Montreal Children's Hospital Foundation.

Key-words: (up to 5):

Key-words: Arsenicals, Kidney organogenesis, Nephrogenesis, In utero exposure, Ureteric bud branching

Abstract #00005341 en

Paternal programming of metabolic alterations in the liver of fetuses sired by diabetic male rats

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Pirrone Irune (1), Schibert Florencia (1), Ranieri Alejandro (1), Jawerbaum Alicia (1), Capobianco Evangelina (1) (1) CEFYBO-CONICET

Background/aims:
Exposure of spermatozoa to paternal diabetes can result in lasting epigenetic modifications that affect fetal development and, in turn, the long-term metabolic health of the offspring. In this context, investigating the fetal liver offers valuable insights into how paternal health conditions may shape the metabolic programming and disease susceptibility of future generations. Aim: to study the paternal programming of alterations in lipid levels and oxidative stress in the liver of fetuses sired by diabetic male rats.

Methods:
Male control and diabetic Wistar rats (obtained by neonatal streptozotocin injection, 90 mg/kg) were mated with healthy females (n=8) (Ethical approval: RESCD-2023-788-E-UBA-DCT#FMED, N°4081/04). On day 21 of gestation, the fetuses were sexed under stereomicroscope and the fetal plasma and liver stored at -80°C to measure lipid levels (by TLC) and lipoperoxidation (by determination of tiobarbituric acid reactive species, TBARS), and the mRNA expression of the antioxidant enzymes Manganese Superoxide Dismutase (Mn-Sod) and Catalase (by qPCR).

Results:
Fetuses sired by diabetic males showed increased triglyceridemia (9.6%, $p<0.05$) and increased liver triglycerides in both sexes (91.1%, $p<0.05$). Liver phospholipids were increased in male fetuses, while free fatty acids were increased in female fetuses sired by diabetic males (46.4% and 75.2%, respectively, $p<0.05$ vs Controls). Additionally, fetuses sired by diabetic males showed increased TBARS in the livers of male fetuses (20.9%, $p<0.05$, vs Controls), but not of females. Male fetuses sired by diabetic males also showed
significantly higher hepatic mRNA expression of Mn-Sod (114%, $p<0.05$ vs Controls), with no significant changes in Catalase mRNA expression. In female fetuses sired by diabetic males, mRNA levels of both Mn-Sod and Catalase showed no significant differences.

Conclusions:
Paternal diabetes programs sex-dependent alterations in lipid levels, oxidative stress and expression of antioxidant enzymes in the fetal liver that can potentially affect the metabolic health of the offspring.

Funding:
Foncyt- PICT 2020-0933.

Key-words: (up to 5):
Fetal programming – paternal diabetes – lipid metabolism – fetal liver – oxidative stress.

Abstract #00005351 en

Advanced maternal age affects FoxO1 regulation in the decidua during placenta formation

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Leonardi María Laura (1), Ranieri Alejandro (1), Recchia Lautaro (1), Jawerbaum Alicia (1), Higa Romina (1) (1) CEFYBO - UBA - CONICET

Background/aims:
Pregnancy at Advanced Maternal Age (~35 years, AMA) is associated with increased risks of adverse pregnancy short- and long-term outcomes. In our rat model of AMA, decreased embryonic growth and altered placental morphology were previously observed on day 12 of pregnancy, a stage in which the decidua plays a critical role in embryo development and placenta establishment. FoxO1 is a transcription factor that plays a role in decidualization and serves as a sensor of ROS. Phosphorylation by AKT and SGK1 induces its inactivation. Previously, we have shown that the activity of FoxO1 was increased in decidua from AMA. Here, we aim to study phosphorylation of AKT and SGK1, lipoperoxidation and mRNA levels of proteins of electron transport chain, in decidua from control and AMA rats.

Methods:
Three-month-old (Control) and ten-month-old (AMA) Wistar rats were mated with three-month-old males (CICUAL-408142021). On day 12 of pregnancy, decidua was obtained (n=7) and AKT and SGK1 phosphorylation were measured by Western blot, lipoperoxidation by TBARS and mRNA levels of Nd1 and Ndufa6 by RT-PCR.

Results:
In the decidua of AMA rats, no differences were detected in total or phosphorylated AKT compared to controls. However, SGK1 phosphorylation was reduced (-48%, $p<0.05$), while total SGK1 levels remained unchanged. Lipoperoxidation (+32%, $p<0.05$) and mRNA levels of Nd1 and Ndufa6, proteins of complex I from electron transport chain, were increased in the decidua of AMA rats compared to controls (+66% and +50% respectively, $p<0.05$).

Conclusions:
These findings suggest that AMA-induced oxidative environment, combined with disrupted SGK1 signaling, may enhance FoxO1 activation, impairing proper decidualization and embryo support in early pregnancy.

Funding:
FONCYT_PICT2021_GRF-0166

Key-words: (up to 5):
Advanced maternal age, placenta, decidua, FoxO1 regulation

Abstract #00005357 en

Maternal obesity programmes an increase in adult offspring cardiac miR-15b-5p and enhances its release in extracellular vesicles after ischemia-reperfusion

Mechanisms Determining Transgenerational Effects of Health and Disease

Cordova Adriana (1), Pantaleao Lucas (1), Niu Youguo (2), Giussani Dino (2), Fernandez-Twinn Denise (1), Ozanne Susan (1)

(1) Institute of Metabolic Science, University of Cambridge, (2) Department of Physiology, Development, and Neuroscience, University of Cambridge

Background/aims:

One of the most common pregnancy complications globally is obesity. Children born to obese pregnancies are at increased cardio-metabolic risk. However, underlying mechanisms remain unclear. Here, we aimed to (1) determine the effect of maternal obesity on offspring cardiac miRNA 15b-5p expression (2) establish if cardiac miRNA 15b-5p could be packaged into extracellular vesicles (EVs) before and after ischemia-reperfusion (IR) and (3) identify target tissues that cardiac EVs could fuse with.

Methods:

We used an established mouse model of maternal obesity and studied offspring at 12-weeks of age. Using a Langendorff preparation, we determined if miR15b-5p was released in EVs from isolated hearts in response to IR. Uptake of labelled cardiac EVs into different cell lines was assessed using high content microscopy. Animal studies were approved by the University of Cambridge Animal Welfare and Ethical Review Board in accordance with the UK Animals Scientific Procedures Act 1986.

Results:

miR-15b-5p levels were increased in hearts of adult mice born to obese dams. Cardiac tissue of obese offspring released more miR-15b-5p during IR, and some of the released miR-15b-5p was contained within EVs. Compared to controls, levels of miR-15b-5p within EVs were also higher in adult mice hearts exposed to maternal obesity. Cardiac-like myoblasts/(H9c2) and umbilical endothelial/(HUVEC), but not preadipocyte/(3T3-L1), cell lines readily internalised DiR-labelled cardiac EVs following timed exposure.

Conclusions:

Our findings suggest that miR-15-5p, a miRNA programmed by maternal obesity, is released from hearts of adult offspring during IR and contained within EVs. These EVs are taken up selectively by cardiac and vascular cell types suggesting possible communication between ischaemic hearts and the peripheral vasculature.

Funding:

This work was supported by British Heart Foundation/[PG/14/20/ 3076, RG/17/12/33167]; Medical Research Council/[MRC_MC_UU_00014/4]. SEO and DAG are members of BHF Cambridge Centre for Research Excellence /[RE/18/1/34212]. AC-C is the recipient of ANID-Chile fellowship/[74220049].

Key-words: (up to 5):

Heart, miR-15b-5p, Extracellular-vesicles, Ischemia-reperfusion, maternal-programming.

Abstract #00005360 en

Association between urban green spaces and blood pressure in Brazilian adolescents: findings from a birth cohort study

Impact of Early Life Exposures and Environmental Pollutants

Carmona Fabio (1), Luiz Vitor (1), Coelho Eduardo (1), Machado Ivan (1), Cardoso Viviane (1) (1) University of São Paulo

Background/aims:
Exposure to green spaces has been associated with improved cardiovascular health, but few studies have explored this relationship in Brazilian youth. This study aimed to evaluate whether residential exposure to urban vegetation correlates with blood pressure (BP) levels and hypertension prevalence in adolescents.

Methods:
This cross-sectional analysis included 3,026 adolescents (11–13 years) from the BRISA birth cohort in Ribeirão Preto, Brazil. Residential greenness was assessed using the Normalized Difference Vegetation Index (NDVI) within 300 m buffers around participants' homes. BP was measured using standard protocols and converted into percentiles according to Flynn (2017). Hypertension was defined as systolic or diastolic blood pressure >95th percentile for gender, age, and height. Associations with NDVI were estimated using mixed linear models for BP and log-binomial models for hypertension, adjusted for sociodemographic, perinatal, and behavioral confounders.

Results:
Higher residential greenness was significantly associated with lower diastolic blood pressure percentiles (β = –10.01, 95% CI: –19.09 to –0.92; p = 0.031), but not with systolic blood pressure percentiles or hypertension prevalence. Higher BMI Z-scores were consistently associated with increased systolic and diastolic BP and greater risk of hypertension. Prenatal care, physical activity, and higher maternal education were protective factors.

Conclusions:
Greater exposure to urban green areas was independently associated with lower diastolic BP in adolescents, supporting the cardioprotective role of green spaces. These findings highlight the need for urban planning policies that promote equitable access to natural environments to improve youth cardiovascular health.

Funding:
This research was supported by CNPq and FAPESP through the BRISA cohort project. Ethical approval was granted by the Research Ethics Committee of the Hospital das Clínicas, FMRP-USP (CAAE 71581023.4.0000.5440).

Key-words: (up to 5):
urban green spaces, adolescents, blood pressure, NDVI, Brazil

Abstract #00005371 en

CoenzymeQ10 ameliorates placenta efficiency in advanced maternal age

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Ranieri Alejandro (1), Leonardi María Laura (1), Pirrone Irune (1), Jawerbaum Alicia (1), Higa Romina (1) (1) CEFYBO-CONICET (School of Medicine, UBA)

Background/aims:
Proper placental function is essential for optimal fetal development and programming. Placental dysfunction is frequently observed in pregnancies at advanced maternal age (AMA, ~35 years in humans) associated with increased obstetric complications. In a previously established rat model of AMA, we observed increased oxidative stress in the decidua and reduced embryo crown-rump length at gestational day 12, prior to placental establishment. Coenzyme Q10 (CoQ10) is a core component in mitochondrial oxidative phosphorylation with antioxidant properties. Here, we aimed to assess whether maternal treatment with CoQ10 could prevent reproductive impairments in AMA rats at term.

Methods:
Young (3-month-old, Control) and aged (10-month-old, AMA) Wistar female rats were mated with young males. CoQ10 (100 mg/kg/day) or vehicle were orally administered from gestational day 1 to 20. Four experimental groups were obtained: Control, Control+CoQ10, AMA, AMA+CoQ10 (N=7 in each group). On day 21, reproductive indexes and fetal-placental morphometric parameters were evaluated. Ethical approval RESCD-2024-1274-E-UBA-DCT#FMED.

Results:
AMA rats exhibited a reduced number of implantation sites (-41.3%, $p<0.01$) and an increased resorption rate (+457.1%, $p<0.001$) compared to controls. These alterations were prevented by maternal CoQ10 treatment (implantation sites:+194.6%, resorption rate:-81.3%, $p<0.001$ vs AMA). Female and male fetuses from AMA dams showed decreased body weight (-22.6% $p<0.001$, -15.2% $p<0.05$ respectively) and increased placental weight (female:+120.7%, male:+124.5%, $p<0.001$), resulting in reduced placental efficiency (fetal-to-placental weight ratio) (female:-35.6%, male:-32.7%, $p<0.001$) relative to controls. Maternal CoQ10 treatment decreased placental weight to values similar to controls (female:-11.3%, male:-15%, $p<0.05$ vs AMA) and improved placental efficiency (female:+128.1, male:+125.3, $p<0.05$ vs AMA), but did not restore fetal body weight.

Conclusions:
Maternal CoQ10 supplementation improves reproductive outcomes and protects against placental dysfunction in AMA pregnancies, enhancing placental efficiency which was not sufficient to normalize fetal growth.

Funding:
FONCYT_PICT2021_GRF-0166 and FONCYT_2021-0078

Key-words: (up to 5):
Advanced maternal age, placenta, CoenzymeQ10

Abstract #00005376 en

Early and intense medical nutrition therapy during pregnancy improves glycemic control and perinatal outcomes: a clinical study

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Perichart-Perera Otilia (1), Hernández-Hernández Larissa (1), Chávez-Méndez Clyo (1), Terrazas-Macedo Sharon (1), Medina-Avilés Cristina (1), Rodríguez-Bosch Mario (1), Rodríguez-Cano Ameyalli M. (1) (1) Instituto Nacional de Perinatología

Background/aims:
Medical nutrition therapy (MNT) is the cornerstone treatment for gestational diabetes (GDM) and type 2 diabetes (DM2) in pregnancy, improving glycemic control and reducing adverse outcomes. AIM: To evaluate whether intensive MNT (more visits) lowers the risk of adverse perinatal outcomes.

Methods:
We studied 243 pregnant women with DM2 (37.4%) and GDM (62.6%) referred for MNT (Jan-Dec 2023). A perinatal nutritionist delivered MNT with a behavioral approach and intensive education every 3-6 weeks. Women self-monitored capillary glucose (targets: fasting/preprandial <95mg/dl, 1h postprandial <140mg/dl) and poor glycemic control (%values outside targets) was recorded. Blood glucose, HbA1C% and adverse outcomes (preeclampsia-PE, preterm birth, macrosomia, low birthweight-LBW, neonatal intensive care-NICU admission), were obtained from institutional records. MNT intensity (visit count) was recorded; ≥5 visits defined intense-MNT. Descriptive statistics, bivariate analysis and multiple logistic regressions were performed.

Results:
Mean age was 33.8±5.8 years; median MNT visits was 3.0 (1-10). The intense-MNT group included more women with DM2 (49.2% vs 33.5%), more insulin users, and earlier MNT initiation (16.8±5.1 vs 27.0±5.7). This group showed lower HbA1c%, a trend toward better glycemic control (last visit), higher gestational age at birth, fewer NICU admissions, and no macrosomia. In multivariable models (R2:0.07-0.20), low-intensity MNT was associated with higher HbA1c% (0.400, 95%CI:0.160 to 0.640) and lower gestational age at birth (-1.040, 95%CI: 1.742 to -0.338). More MNT visits were linked to reduced risk of LBW and NICU admission. Models were adjusted for maternal BMI, diabetes type, gestational age at birth and/or PE. DM2 was associated with more adverse outcomes than GDM.

Conclusions:
Early intense-MNT should be implemented in women with diabetes in pregnancy, as more visits are associated with improved outcomes (glycemic control, gestational age at birth, LBW, NICU admission).
Starting MNT at GDM diagnosis (24-28 weeks) may limit its benefits on perinatal outcomes.

Funding:
None

Key-words: (up to 5):
dietary counseling, metabolic health, prenatal care

Abstract #00005377 en

Site-dependent adaptations in placental gene expression in outbred female mice submitted by low-protein diet

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Nivia-Riveros Jose Andres (1), Felicioni Fernando (1), Alvarenga-Fagundes Ana Maria (1), Meireles Nogueira Julia (1),
Jorge Erika Cristina (1), Radicchi Campos Lobato de Almeida Fernanda (1)
(1) Federal University of Minas Gerais

Background/aims:
Great attention has been given to maternal malnutrition during pregnancy, as fetal development and postnatal health depend on maternal nutritional status and placental function. This study aimed to determine placental gene adaptations according to uterine segment and association with fetal development in outbred mice fed with low protein diet.

Methods:
Female Swiss mice(n=55) were fed either a normal (NPD, 20%crude protein,n=29) or a low protein(LPD,8% crude protein,n=26) diet two weeks before and throughout pregnancy. Dams were euthanized at gestational day 17.5 to evaluate fetal biometrical measurements by sex and placental weight. Moreover, two pools of three placentas each from different dams in the same experimental group were processed and the relative gene expression of nutrient transporters, metabolic regulators and kisspeptin was performed for each uterine segment (Ov:ovary; M:middle portion; Ce:cervix) by real-time quantitative PCR. Data were analyzed using Tukey-Kramer of SAS and relative gene expression analyzes were performed with REST software.

Results:
LPD fetuses and placentae were lighter and shorter regardless of sex and exhibited greater brain-to-liver weight ratio($P<0.05$), providing evidence of intrautertine growth restriction. Greater placental efficiency was more pronounced in LPD males($P<0.05$). Overall gene expression between both experimental groups revealed that LPD up-regulated the SNAT1 and KISS1R expressions in placentas and down-regulated mTOR and IGF2R($P<0.05$). Additionally, differences in gene expression were also observed depending on placental location. Next to the ovary, the expressions of FATP4, mTOR, Kiss1 and STAT3 were up-regulated in LPD placentas($P<0.05$). In the middle portion, SNAT1 and Kiss1 were up-regulated, while SNAT4 was down-regulated in LPD placentas($P<0.05$). LPD placentas close to the cervix showed down-regulation in IGF2R and up-regulation of SNAT1 and KISS1R($P<0.05$).

Conclusions:
The present study provides the first evidence of LPD placental gene expression differences according to uterine segment, suggesting the mechanisms by which the placenta adapts to LPD.

Funding:
Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG)

Key-words: (up to 5):
Placenta, Nutrient transports, Kisspeptin, Low-protein diet, IUGR

Abstract #00005392 en

Postnatal Effects of Maternal Exposure to Subclinical Infection

Impact of Early Life Exposures and Environmental Pollutants

Beltrame Jimena Soledad (1), Scheffer Frida (1), Cañumil Vanesa A. (1), De la Cruz Borthiry Fernanda L. (1), Bogetti Eugenia (1), Franchi Ana M. (1), Ribeiro María Laura (1)
(1) CEFyBO (UBA-CONICET)

Background/aims:
Background/aims: The maternal environment plays a crucial role in fetal development and metabolism, and deficiencies in fetal growth can increase the risk of chronic diseases later in life. In previous studies, we found that low-dose LPS-induced subclinical infections impact fetal growth, affect the vascular processes involved in placentation, and disrupt the balance of pro-inflammatory cytokines and vascular mediators at the maternal-fetal interface. We aimed to investigate the effects of LPS-triggered subclinical infections on the offspring.

Methods:
Methods: For this, we compared the progeny born to control mothers with those born to LPS-treated mothers. We measured different parameters on pups from postnatal day (PND) 4 to PND 21. After weaning, we continued to weigh the pups weekly. We also recorded key developmental milestones and conducted neurodevelopmental tests.

Results:
Results: Maturity indicators such as fur growth, tooth eruption, ear canal opening, and eye opening did not differ significantly between groups. No significant differences were found in weight, anogenital distance, or head size between pups born to control or LPS-treated mothers. However, by PND40, male pups from LPS-treated mothers weighed less than those from control mothers, while female pups showed no weight differences. In the righting reflex test on PND4, female pups from LPS-treated mothers took longer to perform the task than controls, while male pups showed no significant differences. Additionally, a lower percentage of pups from the LPS group displayed mature posture by PND12. No differences were noted in the cliff avoidance and gait tests (PND4), and all pups successfully performed forelimb and hindlimb grasping.

Conclusions:
Overall, LPS-subclinical infections did not affect maturation milestones but impacted neurodevelopment and weight gain, indicating potential lasting effects on offspring.

Funding:
PICT2019 0056 - PICT 2021

Key-words: (up to 5):
SUBCLINICAL INFECTIONS; NEURODEVELOPMENT; POSTNATAL

Abstract #00005399 en

Epigenetic Regulation of MTNR1A and Fn14 Genes and Their Impact on Melatonin and sTWEAK Levels in Preeclampsia: A Case-Control Study

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Kashif Shahid Sana (1), Fatima Syeda Sadia (2), Iqbal Mehir un Nisa (3), Farhat Sabah (4), Khan Shah Jabeen (5)
(1) Department of Physiology, Fazaia Ruth Pfau Medical College, Air University, , (2) Aga Khan Univeristy, (3) University of Karachi, (4) Aga Khan University, (5) Department of Physiology, Fazaia Ruth Pfau Medical College, Air University

Background/aims:
Preeclampsia (PE), a severe hypertensive disorder of pregnancy, affects 1.8–16.7% of pregnancies in developing nations. Placental hypoxia may induce epigenetic modifications that disrupt molecular pathways. Melatonin, an antioxidant, and sTWEAK, an angiogenic mediator, have been linked to PE pathogenesis. This study investigates the methylation status and protein levels of MTNR1A and Fn14 receptors in PE.

Methods:
This case-control study, conducted from June 2022 to November 2023 in Karachi, Pakistan, included 198 pregnant women categorized as normotensive (n=43), high-risk (n=62), or preeclamptic (n=93) based on ACOG 2013 criteria. Venous blood samples were collected at 13–20 weeks gestation and processed for serum and DNA extraction. Serum melatonin and sTWEAK levels were quantified using ELISA kits. DNA methylation of MTNR1A and Fn14 promoter regions was analyzed using bisulfite conversion and methylation-specific PCR.

Results:
Serum levels of melatonin and sTWEAK were significantly reduced in high-risk and PE groups compared to normotensive controls ($p < 0.001$). Hypermethylation of the Fn14 gene was observed in high-risk and PE groups (39.27% ± 0.91% and 38.50% ± 0.71%, respectively) compared to controls (30.97% ± 1.48%). The MTNR1A gene exhibited pronounced hypermethylation in the high-risk (65.56% ± 0.48%) and PE groups (65.42% ± 0.41%) versus controls (54.50% ± 1.72%; $p < 0.001$). These epigenetic alterations correlated with diminished serum protein levels, proposing potential disruptions in angiogenic and antioxidative pathways.

Conclusions:
Hypermethylation of MTNR1A and Fn14 genes correlates with decreased melatonin and sTWEAK synthesis, contributing to PE pathogenesis. Methylation profiling in high-risk pregnancies could serve as an early biomarker for preeclampsia.

Funding:
None

Key-words: (up to 5):
Melatonin, MTNR, sTWEAK, Fn14, Epigenetics, DNA methylation, Preeclampsia

Abstract #00005401 en

Epigenetic Links to Gestational Diabetes: Methylation of Metabolic Genes in Karachi Women

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Fatima Syeda Sadia (1), Mohammed Nuruddin (2)
(1) Aga Khan Univeristy, (2) Aga Khan University

Background/aims:
Women with gestational diabetes mellitus and their offspring have an increased risk of adverse perinatal and long-term health outcomes, which may be attributable to epigenetic modification of diabetes and obesity susceptibility genes. We aimed to investigate the methylation patterns of eight genes in GDM and normoglycemic mothers, and their respective offspring.

Methods:
Cross-sectional study, conducted at Aga Khan University from August 2019-December 2022, recruited pregnant women in the first trimester of gestation from outpatient obstetrics clinic. Participants were classified as NG or GDM based on Society of Obstetricians and Gynecologists Pakistan. Venous blood samples were collected from mothers and cord blood from neonates. Peripheral blood mononuclear cells were used for DNA extraction and methylation analysis using methylation-specific PCR. Maternal and neonatal clinical data were recorded. Statistical analysis was performed using R, including binary logistic regression to assess the association between various gene methylation levels and GDM.

Results:
The study found that GDM mothers had significantly higher fasting blood glucose, 2-hr OGTT, and serum carboxymethyl lysine (CML) levels compared to NG mothers, but no significant differences in neonatal birth weight or serum CML levels. Chemerin methylation was significantly lower in GDM mothers and their babies, while NAMPT, MTNR1B, FNDC5, FAT4, and FTO methylation levels were higher in GDM offspring compared to NG offspring. GDM mothers also had higher methylation levels of brain-derived neurotrophic factor gene (BDNF). Multivariable binary logistic regression identified methylation levels of maternal BDNF and neonatal MTNR1B to be independently associated with GDM.

Conclusions:
Study shows a trend of epigenetic modifications in both GDM mothers and their offspring in various genes related to metabolism and inflammation, suggesting an intergenerational transmission of increased risk of developing metabolic disorders. These findings emphasize need for high throughput studies, early screening, tight glucose control during pregnancy, and postnatal follow-up to mitigate long-term health risks.

Funding:
Aga Khan University Research Council Grant (Project ID: 182111BBS).

Key-words: (up to 5):
advanced glycation end products, gestational diabetes, gene methylation, diabetes mellitus

Abstract #00005403 en

The Flourishing Child: Perceptions and Measures of Flourishing from the Start of Life

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Davis Jacqueline (1), Talati Zenobia (1), Gibson Lisa (1), Silva Desiree (2), Prescott Susan (3)
(1) The Kids Research Institute Australia, (2) University of Western Australia, (3) Nova Institute for Health

Background/aims:
The current narrative surrounding children's health and wellbeing often focuses on adversity and dysregulation with a lack of positive messaging. However, promoting protective and buffering factors may be as important as reducing adverse exposures. The predominant method for identifying young children who need support relies on past experiences (e.g., adversity) or existing outcomes (e.g., delays in health or developmental outcomes). The Flourishing Child study is investigating how we might support children on a flourishing trajectory from the start of life.

Methods:
The Flourishing Child study has several phases: the first is to define childhood 'flourishing' through extensive stakeholder consultation, then undertake a systematic search of the academic and grey literature on conceptualisations and measures of childhood flourishing. The second phase is to co-develop and test a Flourishing Assessment and Pathway Tool for parents of children aged 0-5 years, including those with special needs. The study is nested within a longitudinal population-level cohort, ORIGINS, based in Western Australia. The Flourishing Child study is guided by a consumer panel and stakeholder steering committee.

Results:
For the first phase we collected data through several methods and at sequential timepoints: 496 participants completed an online questionnaire including parents and carers of young children; we ran two focus groups (n=25), and undertook child interviews with 94 5-year olds. Results from this phase enabled us to define child flourishing as, "a measure of child wellbeing that refers to the extent to which a child experiences love, safety, positive lifestyle, fun, happiness, and curiosity."

Conclusions:
This conceptualisation of childhood flourishing lays a theoretical and community informed framework necessary for developing practical tools (phase 2) that will enable parents and carers to assess a child's capacity to flourish across the lifespan.

Funding:
The Flourishing Child study (phase 2) has received funding from the Medical Research Future Fund. ORIGINS has received core funding support from the Telethon Perth Children's Hospital Research Fund, Joondalup Health Campus, the Paul Ramsay Foundation, the Commonwealth Government of Australia through the Channel 7 Telethon Trust and the Stan Perron Charitable Foundation.

Key-words: (up to 5):
Flourishing; childhood; protective; stakeholders; measures

Abstract #00005404 en

Trajectories of Perinatal Maternal Mental Health and Associations with Child Mental and Behavioural Health Outcomes at 3 years of age in the ORIGINS cohort

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Davis Jacqueline (1), Gregory Sonia (1), Bear Natasha (1), Gibson Lisa (1), Silva Desiree (2), Prescott Susan (3) (1) The Kids Research Institute Australia, (2) University of Western Australia, (3) Nova Institute for Health

Background/aims:
Perinatal mental health issues are linked with a range of immediate and long-term negative outcomes for women, children, and families. Early life is a critical period of development offering a unique opportunity to influence lifelong trajectories of growth and wellbeing. To develop effective interventions, it is essential to better understand the causal pathways in prospective, longitudinal studies. Our study aimed to identify trajectories of maternal psychological distress (depression, anxiety and stress) during pregnancy and the postnatal period, and examine their associations with child mental and behavioural health in children at age three in an established Australian longitudinal study.

Methods:
A retrospective analysis using maternal self-report measures collected at multiple antenatal and postnatal time points in the ORIGINS cohort, a longitudinal cohort study, based in Western Australia. ORIGINS is tracking 10,000 pregnant women, their partners, and babies from pregnancy through childhood. Mothers were included in the trajectory analysis if they had measures of psychological distress antenatally and for at least one of the postnatal timepoints. Their children were included if they had behaviour and development data from the Conners Early Childhood (EC) scale at three years of age.

Results:
Among 1442 pregnancies, we identified four trajectories of maternal depression from: “Very Low Stable” (50.4%) to “High Increasing” (7.8%); three trajectories of anxiety from “Low Stable” (59.4%) to “High Increasing” (7.7%); and four trajectories of stress from “Very Low Stable” (21.6%), “to “High Increasing” (11.3%). From the total pregnancies, 510 children exhibited significantly greater scores in the Conners domains of anxiety, mood and affect, and emotional lability, if their mothers belonged to the highest trajectories, compared to the lowest.

Conclusions:
These findings highlight the importance of early risk identification and targeted, personalised mental health support from conception, for the benefit of both mother and child.

Funding:
ORIGINS has received core funding support from the Telethon Perth Children’s Hospital Research Fund, Joondalup Health Campus, the Paul Ramsay Foundation, the Commonwealth Government of Australia through the Channel 7 Telethon Trust and the Stan Perron Charitable Foundation.

Key-words: (up to 5):
Maternal, child, mental health, trajectories

Abstract #00005405 en

ORIGINS: A Platform for Research Discovery

Big Data and Cohorts in DOHaD Research.

Gibson Lisa (1), Davis Jacqueline (1), Whalan Sarah (1), D'Vaz Nina (1), Silva Desiree (1), Prescott Susan (1) (1) The Kids Research Institute Australia

Background/aims:
ORIGINS is the largest study of its kind in Australia, following 10,000 infants from their time in the womb, investigating the prevention of non-communicable diseases as well as discovering how every child, adult, and family can reach their full potential.

Methods:
In addition to observational data, ORIGINS provides a framework for a series of smaller intervention studies nested within the main observational cohort. A series of different studies are integrated within ORIGINS to improve modifiable aspects of the early life environment including nutrition, physical activity, microbial diversity, environmental pollutants (including plastics), green space, blue space, weight gain, language development and mental wellbeing.

Results:
Currently ORIGINS has recruited over 10,000 families (>23,000 participants), collected over 20 million data points and over 400,000 aliquots of biological samples. We have completed 2,800 one-year checks, 1,500 three-year checks and approximately 1,000 five-year assessments, as well as integrating and harmonising over 50 nested sub-projects.

Conclusions:
ORIGINS serves as an example of how a research platform, not only enables local and international research, but provides pathways for prevention, early identification and treatment in children.

Funding:
ORIGINS has received funding support from the Telethon Perth Children's Hospital Research Fund, Joondalup Health Campus, the Paul Ramsay Foundation, the Commonwealth Government of Australia through the Channel 7 Telethon Trust and the Stan Perron Charitable Foundation.

Key-words: (up to 5):
Databank, Biobank, Cohort, Longitudinal, Prevention

Abstract #00005408 en

Smarter Pregnancy App for lifestyle coaching in pregnant women with obesity: protocol for effectiveness in the HYGEIA randomized controlled trial

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Rousian Melek (1), de Bruin Rianne (1), Rosman Ageeth (2), Fabbricotti Isabelle (3), Steegers-Theunissen Regine (1)
(1) Erasmus MC, University Medical Center, (2) Rotterdam University of Applied Sciences, (3) Health Services Management and Organisation, Erasmus University Rotterdam

Background/aims:
Maternal obesity poses a significant public health challenge, increasing the risk of adverse pregnancy outcomes, including cardiovascular and metabolic diseases (CVMD) such as gestational diabetes. Smarter Pregnancy is an evidence-based digital lifestyle coaching program designed to reduce lifestyle-related pregnancy risks. The HYGEIA trial aims to adapt and evaluate the web-based version into the Smarter Pregnancy App (SP App) for pregnant women with obesity. The primary aim is to reduce CVMD incidence; secondary aims include improving maternal and neonatal outcomes, assessing cost-effectiveness, and developing a scalable framework for nationwide implementation within the Dutch healthcare system.

Methods:
HYGEIA is a multicenter randomized controlled trial enrolling 930 pregnant women with a BMI ≥30 kg/m² and a singleton pregnancy of ≤14 weeks gestation. Participants will be randomized to the intervention (n=465) or control (n=465) group. The intervention group will receive six months of personalized coaching via the SP App, plus one/two video consultations. The app provides evidence-based coaching on nutrition, physical activity, mental health, folic acid and vitamin D supplement use, and cessation of smoking and alcohol. The control group will receive standard care.

Results:
The primary outcome - CVMD incidence - is assessed using a composite score including hypertensive disorders of pregnancy, gestational diabetes, and worsening of pre-existing chronic hypertension or diabetes. Secondary outcomes include changes in lifestyle risk scores, maternal and neonatal outcomes and cost-effectiveness. Tertiary outcomes include patient satisfaction, provider feasibility and an implementation roadmap. Data will be collected using validated questionnaires, electronic medical records, time-driven activity-based costing, stakeholder input, guided by the NASSS-framework.

Conclusions:
The HYGEIA trial aims to generate essential evidence on feasibility, effectiveness, and cost-effectiveness of the SP App customized for pregnant women with obesity. If successful, it will replace the online version and support self-management in both clinical care and broader public health settings.

Funding:
ZonMW Leefstijl in de Zorg, the Netherlands, grant number: 10930012310005

Key-words: (up to 5):
Pregnancy, Obesity, Lifestyle, Digital intervention, Cardiovascular

Abstract #00005411 en

Diaphragm phenotype is affected by transient exposure to neonatal hyperoxia: a model of preterm birth-related conditions

Impact of Early Life Exposures and Environmental Pollutants

Poletto Bonetto Jéssica (1), Deprez Alyson (1), Ravizzoni Dartora Daniela (1), Mayrink Pedro Henrique (1), De Sousa do Outeiro Coraline (1), Araujo Natalia (1), Beaulieu-Shearer Alexander (1), Cloutier Anik (1), Dumont Nicolas (1), Nuyt Anne Monique (1)
(1) Sainte-Justine University Hospital and Azrieli Research Center, Université de Montréal

Background/aims:
Individuals born preterm present lower aerobic capacity and inspiratory muscle strength. In animal models, rats exposed to neonatal high O2 levels (O2-related injury - OI) to mimic preterm-birth conditions exhibit peripheral muscle atrophy, fibrosis, fiber typing switch and reduced contractility. However, it remains unclear whether the diaphragm, a key muscle for aerobic performance, is impacted by OI. We aimed to investigate the effects of neonatal hyperoxia on the functional and structural properties of the diaphragm muscle in juvenile rats.

Methods:
Male Sprague-Dawley pups were exposed to 80% O2 (OI) or room air (Ctrl) from postnatal days (P) 3-10. Diaphragms were collected at P10 and P28. We measured diaphragm function, fiber size/type, protein turnover markers, myonuclei and satellite cells number. OI vs. Ctrl were compared using T-test, n= 5-8 rats/group (Ethics approval # 2021-3309).

Results:
Diaphragm weight (0.25±0.02 vs. 0.23±0.02g), excursion (2.3±0.3 vs. 1.9±0.3mm), thickening fraction (20.4±2.2 vs. 15.0±6.0%), and inspiratory velocity (-11.1±1.6 vs. -9.5±1.4mm/s) were decreased in P28 OI rats while expiratory parameters remained unchanged. Despite similar muscle force/fatigue, OI rats had slower time to peak tension (0.12±0.03 vs. 0.07±0.001ms), reduced myonuclei number (1.2±0.12 vs. 1.0±0.04), a significant shift towards smaller fibers size, and increased fast-glycolytic fiber-type IIB (3.81±0.95 vs. 0.19±0.06%). Satellite cell number was similar across groups. Protein turnover assessment at P10 showed lower Akt protein synthesis marker (0.83-fold) in OI rats, remaining unchanged at P28.

Conclusions:
Neonatal hyperoxia induces diaphragm functional and phenotypic changes in juvenile age. Decreased myoblast fusion and protein synthesis might be the underlying mechanisms for the altered myofiber size. Whether diaphragm dysfunction stems from altered intrinsic contractility or from morpho-functional lung changes remains to be studied. Understanding the impact of preterm birth on respiratory muscle, and thus aerobic capacity, is essential to optimize preventive/therapeutic approaches to mitigate the increased risk for chronic diseases in former preterms.

Funding:
Canadian Institutes of Health Research (MFE-181801 and PJT-174993).

Key-words: (up to 5):
Preterm birth, neonatal hyperoxia, diaphragm function, skeletal muscle

Abstract #00005412 en

Maternal childhood adversity is associated with prenatal distress, DNA methylation, and infant attachment

Mechanisms Determining Transgenerational Effects of Health and Disease

Scorza Pamela (1), Mai Christine (2), Berardino Bruno (3), Redondo Julia (4), Cánepa Eduardo (3)
(1) Columbia University, (2) University of Cincinnati College of Medicine, (3) Universidad de Buenos Aires, (4)

Background/aims:
Adverse childhood experiences (ACEs) have detrimental intergenerational health consequences, however mechanisms require elucidation.
Objective: We test the relationship between mothers' ACEs, mothers' prenatal anxiety and depression symptoms, and DNA methylation (DNAm) in maternal prenatal blood and infant umbilical cord blood.

Methods:
Participants and setting: Data were analyzed from 67 women in Buenos Aires, Argentina and a subsample of 24 for DNAm data.
Methods: DNAm was analyzed using Illumina EPIC microarray. Regression analyses assessed the relationships between maternal ACEs and infant attachment, prenatal depression and anxiety, and DNAm age. ANCOVA assessed differential methylation in co-methylated regions (CMRs) between ACE+ and ACEdyads. Genes associated with CMRs with unadjusted p-values below 0.05 were used for gene set enrichment analysis and functional annotation using ShinyGO.

Results:
Maternal ACE score was associated with lower rates of secure attachment at 3 months (OR= .52 p=0.003) and higher prenatal depression (β= 0.84, p=0.004) and anxiety (β = 1.36, p=0.02) symptoms. Prenatal depression and anxiety were not correlated with infant attachment. Maternal ACE score was associated with epigenetic age acceleration in maternal prenatal blood (β =0.49, p= 0.09). Prenatal depression (β = .10, p=0.07) and anxiety (β =.05, p=0.07) were correlated with epigenetic age deceleration in cord blood. No CMR was associated with maternal ACE score at the FDR-corrected p<.05 level. ACE-associated DNAm variation was enriched for genes related to nervous and reproductive systems development.

Conclusions:
ACEs may affect the next generation through maternal mental health, infant attachment, and DNAm, particularly in low or middle-income country settings.

Funding:

Key-words: (up to 5):
DNA methylation, adverse childhood experiences, intergenerational transmission, attachment

Abstract #00005421 en

Maternal chronic consumption of different fat sources affects placental gene expression of cellular nutrient transporters in a sex-dependent manner in heterogenic mice

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Alkmim Tulio Cezar Caiafa de (1), de Almeida Jonathas Medeiros (1), Riveros José Andrés Nivia (1), Jorge Erika Cristina (1), de Almeida Fernanda Radicchi Campos Lobato (1)
(1) Universidade Federal de Minas Gerais

Background/aims:
Maternal nutrition plays a crucial role in determining the health status of both mother and offspring. Fat has received considerable attention due to its availability of long-chain polyunsaturated fatty acids (PUFAs), which are critical for placental development. This study aimed to evaluate the effects of the consumption of three widely consumed dietary fats on the placental expression of specific nutrient transporters genes: SNAT1 and SNAT4 (aminoacids), GLUT1 (glucose) and FATP4 (lipids).

Methods:
Nineteen female Swiss mice were randomly allocated to four experimental groups: CC (control; n= 6); SO (soybean oil; n=4); CO (coconut oil; n=4); and LA (lard; n=5). Animals from each experimental group received daily doses of 0.6mL of the respective fat source through gavage (extra 5kcal/day). At E17.5, mice were euthanized for placental samples collection which were grouped in three biological pools per fetal sex and treatment, followed by RNA extraction and gene expression analysis in technical triplicates using quantitative PCR (qPCR) efficiency (approved CEUA/UFMG/Protocol number 103/2020). Data analyses were performed with REST software (QIAGEN, 2009), using a pairwise fixed reallocation randomization test.

Results:
The results revealed sex-specific effects on placental gene expression transporters. In females, SNAT1 expression increased in SO, while SNAT2 and GLUT1 were downregulated in both SO and LA groups($P<0.05$). In contrast, FATP4 expression remained unchanged($P>0.05$). In males, SNAT1 was also upregulated by SO, while SNAT2 expression decreased in SO and LA groups($P<0.05$). GLUT1 expression was upregulated only in males exposed to SO($P<0.05$), suggesting differential glucose transport dynamics compared to females. Notably, FATP4 expression was significantly elevated in males from the CO group($P<0.05$), indicating a potential adaptive response in lipid transport under low-PUFA dietary conditions.

Conclusions:
These findings demonstrate that maternal dietary fat source modulates the expression of placental nutrient transporters in a sex-dependent manner, which may have implications for fetal nutrient supply and long-term metabolic programming.

Funding:
CAPES - Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior

Key-words: (up to 5):
Placenta, cellular nutrient transporters, coconut oil, soybean oil, lard.

Abstract #00005426 en

Insulin and vitamin D: a strategy on glycemic control and reproductive performance of pregnant diabetic rats

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Barco Vinícius Soares (1), Gallego Franciane Quintanilha (1), Souza Maysa Rocha (1), Paula Verônyca Gonçalves (1), Gomes Maria Eduarda Picolo (1), Volpato Gustavo Tadeu (2), Damasceno Débora Cristina (1)
(1) Botucatu Medical School (FMB), Sao Paulo State University (UNESP), (2) Federal University of Mato Grosso (UFMT)

Background/aims:
Diabetes mellitus is a chronic disease that affects over 580 million adults worldwide, with health expenditure exceeding one trillion dollars, and is expected to rise to 853 million adults by 2045. Diabetes can negatively affect embryofetal development, resulting in vulnerability to diseases in the offspring's adulthood. To improve insulin therapy during pregnancy, this study aimed to evaluate the effects of insulin treatment associated with vitamin D on glycemic levels and reproductive performance of diabetic rats at the end of pregnancy.

Methods:
All procedures were authorized by the Local Animal Use Ethics Committee (#1409/2022). The sample size calculated to 5 animals/group was used. Normoglycemic (Control) and diabetic (Dm - induced by beta-cytotoxic drug) Sprague-Dawley rats were used. Diabetic rats were treated with vitamin D (Dm+VitD), insulin (Dm+Ins), or both (Dm+Ins+VitD) before and during pregnancy. After 15 days of treatment, glycemia was determined, rats were mated, and reproductive performance was determined at the end of pregnancy. $P < 0.05$ was considered a statistically significant level.

Results:
The Dm group showed higher glycemia than the Control group. The Dm+VitD group showed no statistical differences in glycemia and several reproductive performance parameters compared to the Dm group. However, the Dm+Ins group showed reduced glycemia, increased fetal weight, and decreased embryonic death after implantation compared to the Dm group, while the Dm+Ins+VitD rats presented lower glycemia, increased maternal weight gain and placental weight, and decreased embryonic deaths before and after implantation compared to the Dm group, but showed no statistical changes in glycemia compared to the Dm+Ins group.

Conclusions:
The treatment of diabetic rats with insulin and vitamin D before and during pregnancy maintained glycemia and reproductive performance outcomes similar to those of animals treated only with insulin, showing no substantial benefits in diabetes treatment with the addition of vitamin D, which was acquired commercially by pharmaceutical agency donation.

Funding:
Grant 2022/15499-0, São Paulo Research Foundation (FAPESP)

Key-words: (up to 5):
hyperglycemia, rodents, fetal programming, pregnancy, cholecalciferol

Abstract #00005428 en

Cardiovascular evaluation of adult offspring from rats subjected to experimental preeclampsia and supplemented with açaí seed extract

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Nântua Mariana (1), Rodrigues Anchieta Larissa (2), Alencar Cavalheira Mariana (2), Lopes Beserra Silva Dafne (2), Milagres da Silva Anne (2), Pinho dos Santos Gustavo (2), Molinaro da Silva Emilyn (2), Cardoso de Oliveira Beatriz (2), Aguiar da Costa Cristiane (2), Freitas de Bem Graziele (2), De Castro Resende Angela (2), Teixeira Ognibene Dayane (2)
(1) the State University of Rio de Janeiro, (2) Universidade do Estado do Rio de Janeiro

Background/aims:
Preeclampsia (PE), characterized by hypertension and proteinuria after the 20th gestational week, has been linked to an increased cardiovascular risk later in life in mothers and their offspring. Our group previously demonstrated that açaí seed extract (ASE), rich in polyphenols, exhibits antioxidant properties and prevents maternal hypertension and fetal growth restriction in experimental PE. In this study, we aimed to evaluate the effects of maternal ASE supplementation on the cardiovascular system of adult male offspring from rats subjected to L-NAME-induced PE.

Methods:
All procedures were approved by the Ethics Committee for Experimental Animals Use and Care (CEUA IBRAG: 019/2023). L-NAME (60 mg/Kg/d) and ASE (200 mg/kg/d) were administered to pregnant Wistar rats by oral gavage, from gestational day 13 to 20. Animals were divided into four groups (n=6): Control (CT), CT+ASE, L-NAME, and L-NAME+ASE. Male offspring were evaluated at 4 months of age. Blood pressure was measured from 3-4 months of age by tail-cuff plethysmography. At 4 months, vascular reactivity was assessed in aortic rings and mesenteric arterial beds. The aorta and heart were collected for morphometry analyses or immunostaining for AT1 receptors (AT1R) and 8-isoprostane. Malondialdehyde (MDA) and antioxidant enzyme activities were measured in plasma and heart by spectrophotometry.

Results:
Maternal ASE supplementation prevented hypertension ($p<0.0001$) and the increased oxidative damage in plasma, heart, and aorta ($p=0.0386$, $p=0.0361$, and $p=0.0006$, respectively) in male offspring from the PE model, although it did not restore the reduced antioxidant enzyme activities. Additionally, ASE impaired increasing AT1R immunostaining in the heart and aorta ($p=0.0005$ and $p=0.0076$, respectively). No differences were observed in vascular reactivity or cardiovascular morphometry.

Conclusions:
Maternal ASE supplementation protects adult male offspring from developing hypertension in L-NAME-induced PE model. Its beneficial effects are associated with reduced oxidative damage and AT1R expression in the cardiovascular system.

Funding:
CAPES and FAPERJ

Key-words: (up to 5):
L-NAME, Euterpe oleracea Mart., Preeclampsia.

Abstract #00005430 en

EVIDENCE FOR A SEXUAL DIMORPHISM IN PLACENTAL RESPONSE TO LPS-INDUCED MATERNAL IMMUNE ACTIVATION

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Mirón Granese Ayelen Aixa (1), Murillo Murillo Marisol (1), De Laurentiis Andrea (1), Aisemberg Julieta (1), Higa Romina (1), Wolfson Manuel Luis (1), Correa Fernando Gabriel (1) (1) Center for Pharmacological and Botanical Studies - UBA CONICET

Background/aims:
Growing evidence highlights sexual dimorphism in placental function and susceptibility to disorders, with male fetuses demonstrating greater vulnerability to adverse outcomes such as intrauterine growth restriction and preterm birth. Maternal immune activation (MIA) during pregnancy has been implicated in neurodevelopmental programming, yet its sex-specific effects on placental signaling pathways and nutrient transport remain poorly understood. In this study, we investigated how MIA induced by lipopolysaccharide (LPS) administration in CD1 pregnant mice differentially affects male and female placentas.

Methods:
We induced MIA by administering 0.125 mg/ml intraperitoneal of LPS (treated females) or saline (control females) on embryonic day 15.
The experimental procedured reported here were approved by and were carried out in accordance with the Intitutional Committee for the care and use of Laboratory Animals (CICUAL N°4081/04).

Results:
Our results reveal a complex sex-dependent response to MIA. While LPS increased maternal circulating IL-6 levels, we observed a tendency for higher placental IL-6 mRNA expression in female fetuses, contrasting with elevated IL-6 protein levels in amniotic fluid of male fetuses. Intriguingly, basal Akt activation was significantly higher in control female placentas compared to males, and LPS treatment selectively reduced phosphorylated Akt levels only in female placentas ($p<0.05$). Analysis of nutrient transporters showed that MIA differentially affected amino acid transport systems, with SLC38A2 mRNA expression being more markedly reduced in female placentas ($p<0.05$), while SLC38A1 mRNA was upregulated in both sexes. Fatty acid transporter FATCD36 mRNA was downregulated regardless of fetal sex ($p<0.05$), whereas glucose transporter GLUT3 mRNA was downregulated exclusively in female placentas ($p<0.05$) with no changes in GLUT1 mRNA levels in both sexes.

Conclusions:
These findings demonstrate that MIA induces sexually dimorphic responses in key placental pathways, potentially explaining the male-biased vulnerability to adverse pregnancy outcomes.

Funding:
PICT-2022-GRF-TII-00340 **Key-words: (up to 5):**

Sexual dimorphism, maternal immune activation, placental

Abstract #00005432 en

Prenatal exposure to disadvantaged or stressful psychosocial environment associated with adverse infant health and developmental outcomes

Impact of Early Life Exposures and Environmental Pollutants

Bridget BASILE (1)
(1) Yale University

Background/aims:
Significant disparities exist in infant birth outcomes in the United States. Black babies are more than twice as likely to be born low birth weight (LBW) or preterm (PTB), the leading causes of infant mortality. Survivors of preterm birth and babies born at low birth weight also have disproportionately high rates of adverse health outcomes across the lifespan including type 2 diabetes, heart disease, high blood pressure, and learning and behavioral difficulties. Black mothers are more likely to live in disadvantaged psychosocial environments or to experience mistreatment and discrimination. This literature review aims to describe the extant literature describing maternal prenatal and preconception psychosocial exposures and associations with adverse birth outcomes.

Methods:
We employed Smela et al.'s 2023 rapid review methodology.

Results:
138 articles were title/abstract screened and 87 articles were full-text screened. 40 articles were included in the final review. Data extraction was completed by the lead author. The included studies reported significant associations between prenatal stress/adversity and PTB, LBW, and infant development, between socioeconomic deprivation and PTB, LBW, and infant development, between discrimination and infant development, and neighborhood context and PTB and LBW.

Conclusions:
Negative maternal exposures in the prenatal psychosocial environment are associated with increased rates of poor birth and development outcomes including PTB and LBW, the leading causes of infant mortality. Further research is suggested into the biological mechanisms underlying these inequitable outcomes, and to develop tailored interventions to decrease negative birth outcomes.

Funding:
This research was made possible by CTSA Grant Number KL2 TR001862 from the National Center for Advancing Translational Science (NCATS), a component of the National Institutes of Health (NIH), United States.

Key-words: (up to 5):
preterm birth, low birth weight, socioeconomic deprivation, prenatal stress, child development

Abstract #00005442 en

Maternal gut microbiome alterations have lasting effects on offspring metabolomic profiles

Impact of Early Life Exposures and Environmental Pollutants

Parnet Patricia (1), Rastelli Marialetizia (2), Michel Catherine (1), Naour Maxime (1), Grit Isabelle (1), Bouret Sebastien G (2)

(1) Nantes Université, INRAE, UMR 1280, PhAN, IMAD, (2) Development and plasticity of Neuroendocrine Brain , UMR-S 1172, (LilNCog), INSERM

Background/aims:

Recent studies have shown that the maternal gut microbiome (mGM) influences offspring development. As the mGM regulates a variety of circulating metabolites, we investigated how maternal microbiome disruption affects the offspring's metabolome.

Methods:

To this end, we established a mouse model of maternal dysbiosis by administering a broad-spectrum antibiotic (ABX) cocktail during gestation and the first two weeks of lactation and performed microbiota analysis and metabolomics on dams and pups.

Results:

ABX treatment significantly reduced gut bacterial load in dams throughout pregnancy and lactation, without affecting maternal body weight, litter size, or sex ratio. Offspring born to ABX-treated dams exhibited reduced weight gain prior to weaning, followed by catch-up growth post-weaning, associated with increased longitudinal growth. Metagenomic analyses revealed substantial alterations in the composition of the offspring's intestinal microbiome.

We then performed targeted metabolomic profiling of offspring plasma at postnatal day 10 using the Biocrates MxP® Quant 500 Kit. Principal component analysis showed distinct clustering between ABX-treated and control groups, both in dams and their offspring. Using a q-value threshold of < 0.05, we identified several significantly commonly altered metabolites in dams and pups, with 6 small metabolites down regulated between ABX-treated and control groups and 2 small metabolites up regulated. These metabolites were associated not only with microbial metabolism but also with core eukaryotic metabolic pathways, including those involving amino acids and bile acids. Additionally, triglycerides, and other lipid families were significantly up-regulated in ABX-treated pups.

Conclusions:

Our findings suggest that maternal dysbiosis disrupts nutrient availability and key metabolic pathways in the offspring, potentially affecting their energy homeostasis and growth trajectories. Altogether, these results support the hypothesis that the maternal gut microbiome plays a crucial role in shaping early offspring metabolic signatures and developmental outcomes.

Funding:

Agence National pour la Recherche (ANR-22-CE16-0007, MATBIOTA)

Key-words: (up to 5):

maternal gut microbiota, functional analysis, metabolism, growth, metabolomics.

Abstract #00005445 en

Maternal Gestational Diabetes and Infant Adiposity Trajectories: PEAPOD Study

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Gopinath Amitha (1), Periyathambi Nishanthi (2), Bagias Christos (2), Sukumar Nithya (2), Weldeselassie Yonas (3), Saravanan Ponnusamy (2)
(1) George Eliot Hospital NHS Trust, (2) George Eliot Hospital NHS Trust and University of Warwick, (3) School of Mathematics and Statistics, The Open University

Background/aims:
Gestational diabetes mellitus (GDM) affects 5-15% of pregnancies worldwide and is linked to altered fetal growth and increased adiposity risk. While GDM exposure is believed to influence offspring metabolic risk, the early patterns of infant body composition and the role of cord blood biomarkers are not well understood
Objective: This study aims to investigate the relationship between maternal GDM exposure, cord blood metabolic markers, and infant adiposity trajectories during the first six months of life.

Methods:
The PEAPOD study, conducted from 2017 to 2020, included 979 mother-infant pairs (120 exposed to GDM) at a secondary hospital. At delivery, umbilical cord blood was collected to analyse glucose-regulatory hormones (insulin, C-peptide), adipokines (leptin, adiponectin), and inflammatory markers. Infant body composition was measured using air-displacement plethysmography at birth, 1 month, and 5 months. Maternal clinical data, glycemic control, treatment methods, and infant feeding practices were documented. Linear mixed models and mediation analyses were used to explore the associations between GDM exposure, cord blood biomarkers, and infant adiposity trajectories.

Results:
The study found that infants exposed to GDM had significantly faster early adiposity trajectories compared to unexposed infants, with a relative risk (RR) of 3.21 (95% CI: 1.23, 8.35) for fat mass index gain. Infants born to GDM mothers showed a 21.1% faster fat mass increase compared to those born to mothers with normal glycemic status in the first five months of life. No significant association between cord leptin and adiponectin on fat mass gain was observed.

Conclusions:
Infants exposed to GDM exhibited accelerated fat mass index trajectories, adjusted for linear growth. Understanding the biological mechanisms linking maternal GDM exposure to early infant adiposity changes could help develop targeted preventive strategies during pregnancy and early infancy to improve long-term metabolic health outcomes in at-risk children.

Funding:
National institute for health research and Sir Jules Thorns funds

Key-words: (up to 5):
fat mass, adipokines, Gestational diabetes

Abstract #00005451 en

Development of a risk score for periconceptional maternal vulnerability and its association with embryonic growth: The Rotterdam Periconception Cohort

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Wieles Teuntje (1), Bijma Hilmar (1), Smith Sharissa (1), Voskamp Lotte (1), Willemsen Sten (1), Steegers-Theunissen Régine (1)
(1) Erasmus Medical Center, Rotterdam

Background/aims:
Maternal health and exposure to vulnerability factors (i.e. lifestyle, mental health and environmental factors) during the periconceptional period is critical for embryonic development. This study aims to develop a composite Periconceptional Vulnerability Risk Score (PVRS) and examine its association with embryonic growth trajectories.

Methods:
This study included 638 pregnancies from the Rotterdam Periconception Cohort (2010-2020). Data on nine vulnerability factors were collected via questionnaires. The PVRS was calculated using weighted estimates of associations between these factors and Big-3 pregnancy outcomes (congenital anomalies, preterm birth, and small for gestational age). Embryonic growth was assessed through crown-rump length (CRL) and embryonic volume (EV) at 7, 9, and 11 weeks using 3D transvaginal ultrasound and VR software.
Linear mixed models were used to analyze the association between PVRS and embryonic growth.

Results:
The PVRS ranged from -0.071 to 0.320. A higher PVRS was significantly associated with reduced embryonic growth (CRL: β = -0.58 mm, p = 0.001; EV: β = -0.31 cm^3, p = 0.001). Subgroup analyses showed significant associations in naturally conceived pregnancies (CRL: β = -0.82 mm, p = 0.015; EV: β = -0.39 cm^3, p = 0.015) and women with BMI ≥25 (CRL: β = -0.91 mm, p = 0.006; EV: β = -0.51 cm^3, p = 0.001).

Conclusions:
The PVRS is negatively associated with embryonic growth, particularly in naturally conceived pregnancies and women with BMI ≥25. These findings highlight the importance of periconceptional vulnerability assessment and optimization of (modifiable) vulnerability factors.

Funding:
This study was funded by the Department of Obstetrics & Gynecology, Erasmus Medical Center, Rotterdam.

Key-words: (up to 5):
conceptional vulnerability, embryonic growth, risk score

Abstract #00005455 en

Remission of Childhood Overweight and Adult Coronary Heart Disease

Big Data and Cohorts in DOHaD Research.

Kindblom Jenny (1), Bramsved Rebecka (2), Bygdell Maria (2), Martikainen Jari (2), Rosengren Annika (2), Ohlsson Claes (2)
(1) Sahlgrenska Academy and Sahlgrenska University Hospital, (2) Sahlgrenska Academy

Background/aims:
Childhood overweight is associated with adult coronary heart disease (CHD). To which extent this risk can be mitigated by remission of childhood overweight before young adulthood has not been examined.

Methods:
Weight and height data from school healthcare records (at 7-8 and 18-20 years of age, respectively) was collected for all children born 1945-1968 in Gothenburg, Sweden, and from the conscription register. Information on incident CHD was retrieved from national registers. Hazard ratios were estimated using Cox proportional hazards regression. All relevant ethical considerations have been met. The Ethics Committee of the University of Gothenburg, Sweden approved the study

Results:
We included 45,965 women and 57,267 men born 1945-1968. During 3,897,423 person-years of follow-up, a CHD event was recorded in 4,438 men and 1,298 women. Childhood and young adult overweight were associated with increased risk of CHD in both men and women. No significant sex interaction was observed for these associations. Remission of childhood overweight before young adulthood resulted in a similar risk of CHD as in individuals who had never been overweight (=reference, hazard ratio [HR] 0.98, 95% confidence interval [CI] 0.84 to 1.15). Both pubertal onset overweight (i.e. normal weight in childhood and overweight in young adulthood) and persistent overweight (i.e. overweight in both childhood and young adulthood) were associated with increased risk of adult CHD events. However, individuals with pubertal onset overweight had higher risk of CHD events than individuals with persistent overweight.

Conclusions:
The increased risk of CHD in individuals with childhood overweight is reversed with remission of overweight before young adulthood. Furthermore, pubertal onset overweight is associated with higher risk of adult CHD.

Funding:
This study was supported by the Swedish Research Council, the Heart-Lung Foundation, grants from the Swedish state under the agreement between the Swedish government and the county councils, the ALF-agreement, the Yngve Land Memorial Foundation.

Key-words: (up to 5):
Childhood overweight, coronary heart disease, cohort study

Abstract #00005457 en

EFFECTS OF WESTERN DIET AND CAFFEINE ON OVARIAN MORPHOPHYSIOLOGY IN HETEROGENEOUS MICE

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

fERREIA João Vitor (1), Oliveira Pires Dayanne Kelly (2), Caiafa Tulio Cezar (2), Jorge Erika (3), Alvarenga Fagundes Ana Maria (3), Radicchi Campos Lobato de Almeida Fernanda (2)

(1) Graduate Program in Cell Biology/ Federal University of Minas Gerais, (2) Laboratory of Structural Biology and Reproduction (LABER), Federal University of Minas Gerais (UFMG), (3) Laboratory of Oral and Developmental Biology (UFMG)

Background/aims:

The Western dietary pattern is associated with obesity, diabetes mellitus, hypertension, and subfertility. Caffeine, widely consumed worldwide, is used in anti-obesity therapies, but its effects on reproductive health, especially when combined with a Western diet, are often overlooked. This study aimed to investigate the impact of caffeine and a high-fat/high-sugar (HF/HS) diet, associated or not, on ovarian morphophysiology.

Methods:

Twenty female Swiss mice were equally divided into four experimental groups: CC (standard diet + no caffeine), CA (standard diet + 120mg/kg/day caffeine), HC (HF/HS diet + no caffeine), and HCA (HF/HS diet + 120 mg/kg/day caffeine). The standard diet contained 10% lipids and 0% sucrose, while the HF/HS diet included 45% lipids and 17% sucrose. Body weight was monitored weekly; estrous cycles were assessed; ovarian histomorphometry was performed to evaluate follicle population; and ovarian gene expression was analyzed to assess follicle development. Data were analyzed using ANOVA (SAS), with Tukey-Kramer post hoc testing. Ethical approval: CEUA/UFMG 18/2023.

Results:

The CA group showed a reduction in preantral follicles and increased expression of ACVR1, Caspase-3, and BAX($p<0.05$), indicating follicular loss triggered by ACVR1 activation followed by apoptosis. The HC group had the highest number of antral follicles($p<0.05$), a greater proportion of blood vessels, and increased IGF1R expression, suggesting ovarian response to high glucose intake. The HCA group, despite no histological changes, exhibited reduced expression of LHCGR, FSHR, IGF1R, and ACVR1($p<0.05$), indicating decreased ovarian responsiveness to folliculogenesis-related genes, potentially compromising follicle quality.

Conclusions:

Both caffeine and HF/HS diet intakes negatively affect ovarian histophysiology. However, their combination exerts a more pronounced impact on folliculogenesis-related genes and should be avoided to preserve reproductive health.

Funding:

Conselho Nacional de Desenvolvimento Científico e Tecnológico - CNPq

Key-words: (up to 5):

Folliculogenesis, western diet, caffeine, ovary, PCR

Abstract #00005458 en

Lactiplantibacillus plantarum 299v counteracts adverse effects in mother caused by protein-restricted diet consumed during pregnancy and lactation

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Castro Rodríguez Diana Catalina (1), Sandoval Valencia Berenice Lilian (2), Contreras Escamilla Mariela (1),
Zambrano Elena (1), Reyes Castro Luis A. (1)
(1) Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubiran, (2) Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán

Background/aims:
A maternal low-protein (LP) diet leads to offspring (F1) metabolic problems. Maternal probiotic supplementation might be a novel approach to counteract these effects. The aim was to analyze the impact of Lactiplantibacillus 299v, by LP rats on maternal parameters.

Methods:
Mothers were divided into 2 groups: during pregnancy and lactation, the control group (C) was fed a diet containing 20% casein, and the LP group was fed an isocaloric diet with 10% casein. Half the C and LP mothers received a daily dose of probiotic orally (1 x 1010 CFU/mL) through pregnancy and lactation (CP and LPP). Body weight, percent of fat, glucose, cholesterol and triglyceride serum concentrations and morphological adaptive changes of small intestinal (jejunum) were determined in mothers.

Results:
The dams of the four groups weighed the same at the end of lactation, but LP and LPP reduced their intake during lactation due to cannibalism caused by lack of protein in their diet. The LP group had the lowest number of offspring at the end of lactation. Regarding serum metabolic parameters, insulin and HOMA were higher in LP compared to C, CP and LPP ($p<0.05$). Cholesterol levels were higher in LPP compared to C, CP and LP ($p<0.05$). Regarding morphological changes in the jejunum, CP and LPP had higher villus height and more goblet cell production in LP and LPP ($p<0.05$).

Conclusions:
The results show the adverse effect of LP on the metabolism and maternal physiology of Wistar rats, an effect that is counteracted by the consumption of Lactiplantibacillus 299v. It is evident that the consumption of the probiotic prevents metabolic damage in the mothers and, consequently, negative damage in the offspring.

Funding:
CONAHCYT-México (ID73198), and Programa Anual de Adquisiciones; PAA: 2023–2024, INCMNSZ.

Key-words: (up to 5):
Low-protein; programming; probiotic, metabolism, supplementation

Abstract #00005460 en

Epigenome-wide association study of early-life nutrition supplementation among Guatemalan adults

Impact of Early Life Exposures and Environmental Pollutants

Chapnick Melissa (1), Yu Elaine (2), Smith Alicia (3), Conneely Karen (3), Ramírez-Zea Manuel (4), Qin Zhaohui (1), Staimez Lisa (1), Vaccarino Viola (1), Stein Aryeh (1)
(1) Emory University Rollins School of Public Health, (2) Vitalant Research Institute, (3) Emory University School of Medicine, (4) Institute of Nutrition of Central America and Panama (INCAP)

Background/aims:
Persistent differential methylation has been observed following prenatal famine exposure but little is known concerning methylation following nutritional supplementation.

Methods:
We analyzed data from participants in the INCAP Nutrition Supplementation Trial, conducted in 4 villages in eastern Guatemala from 1969-1977. Two villages received atole, a protein-energy supplement, and two received fresco, an energy-only supplement. DNA methylation was measured using the MethyationEPICv2 array and standard quality control procedures from buffy coat samples collected at mean age 45y.

We used intent-to-treat difference-in-difference modeling to assess the impact of atole exposure during 'all' or 'part' of the 'first 1,000 days' (conception to age 2y) on differential methylation patterns across the epigenome. We also examined specific CpG sites within the IGF2 and INSR genes, previously associated with prenatal famine exposure. Covariates included sex, birth year, and a random effect for chip. To account for multiple comparisons, we applied Benjamini-Hochberg false discovery rate (FDR) correction with a 0.05 significance threshold. Analyses were performed in R (version 4.4.0) using CpGassoc.

Results:
The analysis included 1,079 participants (60.2% female). Of the 854,790 CpG sites tested, 30,220 were differentially methylated among those exposed to atole throughout 'all' of the first 1,000 days, and 31,266 among those with 'partial' exposure; 4,636 were associated with both 'all' and 'partial' exposure. No sites remained significant after FDR correction.

A total of 264 CpG sites on the array are located within the IGF2 and INSR genes. Of these, 4 were significantly associated with atole exposure during 'all' of the first 1,000 days, and 7 with 'partial' exposure. One site, cg10738016, was associated with both 'all' and 'partial' exposure.

Conclusions:
We found moderate differences in DNA methylation associated with atole exposure during the first 1,000 days of life, but none of the analyzed CpG sites reached the genome-wide significance threshold.

Funding:
This research was supported by NIH R01 Adult epigenetics and telomere length in relation to improved nutrition in early life (R01 DK134509), NIH R01 Early childhood nutrition and adult metabolomic and cardiometabolic profiles (R01

HD075784), and the NIH T-32 training grant Multidisciplinary Research Training to Reduce Inequalities in Cardiovascular Health at Emory University (T32 HL130025).

The authors confirm that all requirements for abstract submission to the 13th World Congress of the International Society for Developmental Origins of Health and Disease have been met. This study was approved by the Institutional Review Boards at both Emory University and the Instituto de Nutrición de Centro América y Panamá (INCAP). The authors declare no conflicts of interest.

Key-words: (up to 5):
epigenetics, early-life nutrition

Abstract #00005463 en

Gestational Weight Gain in the First and Third Trimesters as Predictors of Neonatal Fat Mass Percentage

Impact of Early Life Exposures and Environmental Pollutants

Mendoza-Ortega Jonatan (1), Rodríguez-Cano Ameyalli (2), González-Ludlow Isabel (3), Suárez-Rico Blanca (4), Rodríguez-Hernández Carolina (2), Acevedo-Gallegos Sandra (5), Tolentino-Dolores Maricruz (2), Sánchez-Martínez Maribel (6), Estrada-Gutierrez Guadalupe (6), Perichart-Perera Otilia (2)

(1) Department of Immunobiochemistry, National Institute of Perinatology, Mexico City 11000, (2) Nutrition and Bioprogramming Coordination, National Institute of Perinatology, (3) Community Interventions Research Branch,
National Institute of Perinatology, , (4) Community Interventions Research Branch, National Institute of Perinatology, (5) Department of Maternal-Fetal Medicine, Instituto Nacional de Perinatologia, (6) Department of Immunobiochemistry, National Institute of Perinatology

Background/aims:
Maternal metabolic status during pregnancy plays a crucial role in maternal-fetal health and may influence the long-term programming of offspring health. Gestational weight gain (GWG) may be associated with adverse maternal metabolic conditions and lasting impact on neonatal body composition. However, there is limited evidence on the trimester-specific effects of GWG on neonatal fat mass percentage, and on how these may interact with maternal metabolic biomarkers. To assess the association between maternal weight gain during the first and third trimesters of pregnancy and neonatal fat mass percentage, and to explore potential interaction effects with maternal glucose, insulin, and triglyceride levels.

Methods:
A total of 94 mother-infant pairs from the OBESO cohort in Mexico City (IRB INPer 2024-1-14) were included. Neonatal fat mass percentage was assessed at birth. Maternal sociodemographic and clinical data were collected, and metabolic parameters (glucose, insulin, and triglycerides) were measured during pregnancy. Linear regression models were used to estimate associations between GWG and neonatal fat mass percentage, adjusted for disease in pregnancy, average energy intake and neonatal length.

Results:
Excessive weight gain during the first trimester was significantly associated with a higher neonatal fat mass percentage (β = 0.33; CI95%=0.09,0.56; p = 0.006). Similarly, third-trimester GWG was positively associated with neonatal fat mass (β = 0.17; CI95%=0.001,0.32; p = 0.044). None of the metabolic or adjustment variables were significant.

Conclusions:
Gestational weight gain in both the first and third trimesters is associated with increased neonatal fat mass percentage, independently of maternal glucose, insulin, and triglyceride levels. These findings highlight the importance of nutritional care and close monitoring of gestational weight gain throughout pregnancy to support optimal offspring metabolic outcomes.

Funding:
This study was supported by the Instituto Nacional de Perinatología (Grant 3300-11402-01-575-17 to

G.E-G.)

Key-words: (up to 5):
Gestational Weight Gain, Neonatal Fat Mass, Maternal Metabolic Biomarkers, Pregnancy

Abstract #00005471 en

Knowledge, attitudes, and practices related to the Developmental Origins of Health and Disease (DOHaD) among perinatal healthcare professionals in Mexico

Public Health Policies Across the Life Cycle.

Gomez-Zapata Hector-Manuel (1), Lopez-Enriquez Jesus-Emiliano (2), Barbosa-Sabanero Gloria (3), Davalos-Perez Adriana (4), Monroy-Valle Michele (5), Hernandez-Gonzalez Martha-Alicia (2), Lazo-de-la-Vega-Monroy Maria-Luisa (3)
(1) IMSS, Mexican Institute of Social Security, (2) Department of Medicine & Nutrition, Health Sciences Division, University of Guanajuato, Leon Campus, (3) Department of Medical Sciences, Health Sciences Division, University of Guanajuato, Leon Campus, (4) Infirmary & Obstetrics Dept., Health Sciences Division, University of Guanajuato, Leon Campus, (5) University of Saskatchewan, Canada/USAC, Guatemala College of Pharmacy and Nutrition

Background/aims:
Developmental Origin of Health and Disease (DOHaD) states that parental health influences the offspring's risk of non-communicable diseases in later life. We aimed to investigate the knowledge, attitudes, and practices (KAP) related to DOHaD in healthcare professionals caring for population in the perinatal period in Mexico to identify potential areas of opportunity for translating the DOHaD concepts into clinical practice.

Methods:
We applied a previously validated online KAP survey to health personnel caring for the population in the perinatal period within all hospital hierarchies, including medical residents, professional practitioners, medical managers, and nursing staff, in public hospitals in Mexico. The corresponding ethics committees approved the study: CIBIUG-P43-2021, and SIRELCIS R-2023-1002-075.

Results:
Of the 194 participants, approximately three quarters (71.6%) knew about the "DOHaD concept". From the total, 88 were obstetricians, (21.5% of them knew DOHaD) and 16 were pediatricians (31.2% of them knew DOHaD). Only 54.1% of the total participants identified the "1000 days concept". More than 30% of participants do not provide patients with information related to the related to DOHaD concept. Only 22.1% considered that they have enough preparation to advise patients concerning DOHaD, and 81.4% think that training health professionals in DOHaD is necessary.

Conclusions:
Although DOHaD approach in research has increased in Latin America, bridging the gap between DOHaD research knowledge and the clinical application still remains challenging. However, healthcare providers' training, particularly in the first years of medical education could improve clinical practices oriented to provide better preventive healthcare.

Funding:
Not applicable.

Key-words: (up to 5):
Medical education, Preventive health, DOHaD, first 1000 days, KAP

Abstract #00005473 en

Gestational caloric restriction alters offspring's brain mitochondrial dynamics

Mechanisms Determining Transgenerational Effects of Health and Disease

Zanella JV (2), Stone V (3), Silva VF (4), Santos B (4), August PM (5), Gayger-Dias V (6), Gonçalves CA (4), Matté C (2)
(2) Departamento de Bioquímica, Instituto de Ciências Básicas da Saúde, UFRGS, (3) Programa de Pós-Graduação em Ciências Biológicas – Bioquímica, ICBS, UFRGS., (4) Programa de Pós-Graduação em Ciências Biológicas – Bioquímica, ICBS, UFRGS, (5) [2]Programa de Pós-Graduação em Ciências Biológicas – Bioquímica, ICBS, UFRGS, (6) [1]Departamento de Bioquímica, Instituto de Ciências Básicas da Saúde, UFRGS

Background/aims:
Caloric restriction (CR) is well recognized for enhancing metabolic health and reducing the risk of chronic diseases. However, its effects when applied during pregnancy—particularly on fetal brain mitochondrial development—are still unclear. This study aims to investigate the impact of gestational CR on cell signaling pathways related to mitochondrial function and antioxidant defenses in the offspring's prefrontal cortex, in order to better understand its role as a non-pharmacological strategy to protect against chronic non-communicable diseases (CNCDs)

Methods:
Pregnant Wistar rats were submitted to 20% CR throughout gestation, supplemented with micronutrients. Male offspring were sacrificed in early adulthood for prefrontal cortex collection. Protein levels of SIRT1, SIRT3, TFAM, PGC1α, AMPK, AKT, Mitofusin, DRP1 and NRF2 were evaluated by western blot. The project was approved by the Ethics Committee of UFRGS (protocol nº 38809)

Results:
Offspring exposed to gestational CR showed decreased levels of SIRT3 ($p=0.0226$) and TFAM ($p=0.0479$) in the prefrontal cortex. No significant changes were found for SIRT1 (nuclear and cytoplasmic), AMPK, Akt, PGC1α (nuclear and cytoplasmic), mitofusin, DRP1 or NRF2 expression ($p>0.05$). These findings contrast with previous data from our lab, which demonstrated enhanced mitochondrial and antioxidant function under similar conditions.

Conclusions:
Moderate gestational CR appears to impact brain mitochondrial regulation in offspring by reducing key markers such as SIRT3 and TFAM. These changes may affect mitochondrial biogenesis and function, potentially influencing long-term neurodevelopmental outcomes. Our findings underscore the dual nature of CR in development—offering both protective and potentially adverse effects—and reinforce the need for further mechanistic studies to inform maternal nutrition strategies that optimize offspring brain health

Funding:
This research was supported by CNPq, FAPERGS, and PROPESQ/UFRGS

Key-words: (up to 5):
Caloric Restriction, Pregnancy, Mitochondria, Prefrontal cortex

Abstract #00005477 en

Miscarriages and hypothyroidism in Argentine rural towns surrounded by pesticide treated agricultural land

Impact of Early Life Exposures and Environmental Pollutants

Verzeñassi Damián (1), Fernández Facundo (2), Madanes Daniela (3), Etchegoyen Agustina (4), Vallini Alejandro (5), Hough Guillermo (6)

(1) Instituro de Salud Socioambiental FCM UNR, (2) Instituto de Salud Socioambiental, Facultad de Ciencias Médicas Universidad Nacional de Rosario, (3) Instituto Nacional de Parasitologia ANLIS Dr Carlos Malbran Ministerio de Salud de la Nación, (4) Escuela Superior de Medicina, Universidad Nacional de Mar Del Plata, (5) Clinica Ambiental Sede Argentina CEI Universidad Nacional de Rosario, (6) ConCiencia Agroecologica Comisión de Investigaciones Científicas de la Provincia de Buenos Aires

Background/aims:

These were to analyze epidemiological data of communities exposed to agricultural pesticides (AP) spraying, focusing on miscarriages, hypothyroidism (HYP) indexes, and their correlation.

Methods:

A house-to-house health survey conducted by last-year medical students was implemented in 9 rural towns of the Province of Santa Fe- Argentina (9T), each surrounded by fields sprayed with AP. 6497 women aged between 18 and 70 years were surveyed, reporting miscarriages and if they were taking HYP medication.

Results:

Total number of pregnancies during the 2008-2018 period in the 9T was 2954, of which 2571 (87%) resulted in births and 383 (13%) in losses, 290 of which were first trimester miscarriages. Estimated first trimester miscarriages in 2008 and 2018 were 7.2% and 16.4% of total pregnancies, respectively. The prevalence of HYP was 11.9%, significantly higher than values reported in other locations. The age-corrected relative risk of suffering a miscarriage if having versus not-having HYP was 1.57 (95% CI= 1.10 - 2.25). The prevalence of HYP in 2018 was 2.5 times higher than in 2008, showing a similar pattern of increase to that of first-trimester miscarriages.

Conclusions:

Our findings suggest that living in small rural communities affected by nearby AP applications has a negative impact on women's health due to the increased likelihood of experiencing miscarriages, as well as having high rates of HYP. These results contribute to the need for AP reduction policies, especially in the vicinity of small urban populations.

Funding:

without external financing

Key-words: (up to 5):

Agricultural pesticides - Miscarriages - Hypothyroidism – Epidemiology - Survey

Abstract #00005478 en

Preconceptional Empagliflozin Treatment Mitigates Placental Dysfunction and Fetal Growth Restriction in a Rat Model of Preeclampsia

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Barrientos Gabriela (1), Higa Claudio (2), Creta Victoria (2), Robello Elizabeth (3), Galleano Monica (3), García Silvia I (4)

(1) Laboratorio de Medicina Experimental, Hospital Alemán; CONICET, (2) Servicio de Cardiología, Hospital Alemán, (3) Instituto de Bioquímica y Medicina Molecular (IBIMOL), UBA-CONICET, (4) Instituto de Investigaciones Médicas (IDIM), UBA-CONICET

Background/aims:

Chronic hypertension in the Stroke-prone Spontaneously Hypertensive Rat (SHRSP) is associated with development of a preeclampsia (PE)-like syndrome and fetal growth restriction. Here, we aimed at evaluating the effect of preconceptional treatment with empagliflozin (EMPA, a sodium-glucose cotransporter 2 inhibitor) on maternal signs, fetal phenotype and placental function in this model

Methods:

All animal research was conducted according to international guidelines and approved by the institutional animal care committee at Hospital Alemán. SHRSP females (6 week-old, n=10-11/group) were randomly assigned to two groups: EMPA, treated for 6 weeks with 1% EMPA (30 mg/kg) in the drinking water, administered ad libitum; and Control, receiving regular tap water. After treatment, syngeneic timed pregnancies were established with vaginal plug detection considered as gestation day (GD)1. Animals were maintained on regular tap water, and maternal blood pressure and glycemia were monitored non-invasively throughout the experiment. Fetoplacental and kidney specimens were collected on GD20 for histology and gene expression analyses. Student's T- or Mann-Whitney U-tests were used for statistical comparisons, with significance set at $p< 0.05$.

Results:

Compared to controls, EMPA-treated dams showed no differences in blood pressure, glycemia or weight gain throughout the experiment. Urinary protein levels, however, were significantly reduced upon EMPA treatment. Notably, EMPA normalized the fetal growth restriction phenotype, leading to increased weights (control 1.96±0.17 g vs. EMPA 2.43±0.35 g, $p<0.0001$) and decreased cephalization indexes. This was associated with an improved placental efficiency (noted as the fetal to placental weight ratio, control 5.19±0.57 vs. EMPA 6.33±0.81, $p<0.0001$), increased vascular density of the labyrinth and decreased intraamniotic levels of TBARS

Conclusions:

Preconceptional EMPA improved maternal signs and mitigated fetal growth restriction in a rat model of PE, emerging as a promising alternative for management of high-risk pregnancies

Funding:

Agencia I+D+i Grant PICT 2020-03263, Sociedad Argentina de Cardiología, Fundación Florencio Fiorini **Key-words: (up to 5):**

sglt2 inhibitor, preeclampsia, placental dysfunction, fetal growth restriction

Abstract #00005481 en

Female Offspring of Obese Rats Display Increased Vulnerability to the Obesogenic Effects of 3MC on the Liver

Impact of Early Life Exposures and Environmental Pollutants

Labiano Marina (1), Dechamps Victoria (1), FLores Quiroga Jeremias Pablo (1), Heinecke Maria Florencia (1), Galarza Rocio (2), Cortez Analia (3), White Veronica (1)
(1) CEFYBO - CONICET, (2) CEREGeo-FCyT-UADER, Facultad de Ciencia y Tecnología, Universidad Autónoma de Entre Ríos,, (3) FMED - UBA

Background/aims:
Previously, the offspring from rats with obesity displayed an increased response to 3-methylcholanthrene(3MC), a polycyclic aromatic hydrocarbon pollutant with toxic and obesogenic effects through the activation of the Aryl Hydrocarbon Receptor(AHR)/To evaluate whether the offspring from rats with obesity had also an increased response to 3MC regarding biotransformation processes, lipid content and damage in their livers

Methods:
Female Wistar rats were fed either a standard chow diet (SD rats) or a high-fat diet (FD rats), mated with control males and allowed to give birth and nurse. Offspring from SD and FD rats were then fed a standard diet. At postnatal day 60, female SD and FD offspring received either 3MC (0.5 mg/kg) (SD3MC and FD3MC) or corn oil as vehicle (SDV and FDV) by oral gavage, three times per week for seven weeks and then euthanized and their livers and serum obtained. Liver lipoperoxidation was assessed by the TBARS, lipid content by thin layer chromatography, AHR protein expression by Western Blot and circulating levels of interleukin 1 (Il1) by EIA

Results:
3MC treatment induced different effects in SD and FD offspring. Hepatic triglycerides content, increased in FDV offspring(382,6%) compared to SDV, was unchanged in SD3MC but decreased in FD3MC(71,6%) compared to FDV. Lipid peroxidation was increased by 3MC in both SD(66,7%) and FD(59,5%) offspring. AHR protein levels were upregulated in the FDV offspring(115,9%) compared to SDV and in SD3MC(33,3%) and FD3MC(40,7%) compared to SDV and FDV respectively. Additionally, 3MC increased the serum IL-1β levels in FD3MC compared to FDV but were unchanged in SD3MC compared to SDV offspring

Conclusions:
Maternal obesity programs an increased susceptibility to 3MC exposure, it increases liver damage probably due to an increased expression of AHR, revealing the role of early-life exposures in the vulnerability to obesogens

Funding:
PICT-2020-SerieA-nº01125/PICT-2021-nºI-A-00281-PIP-2022/23-n°068-CONICET
Ethical-approval:CICUAL-n°549/12-2020

Key-words: (up to 5):
Maternal obesity-3MC-AHR-liver damage-programming

Abstract #00005482 en

Study of the placental consequences of gestational hypercholesterolemia and the effect of extra virgin olive oil in a murine model

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Ríos Vanessa (1), Riquelme Nicolas (1), Morales Andrea (1), Saavedra Fujiko (2), Illanes Sebastian (2), Busso Dolores (2), Leiva Andrea (1)
(1) Universidad San Sebastián, (2) Universidad de los Andes

Background/aims:
During pregnancy, total cholesterol (TC) levels physiologically increase to meet the fetus's nutritional needs. However, a quarter of women develop maternal supraphysiological hypercholesterolemia (MSPH), which is associated with increased oxidative stress, pro-atherogenic lipoproteins, and higher cardiovascular risk. Offspring of MSPH mothers show increased oxidative and vascular damage, promoting atherosclerosis and future cardiovascular disease. Extra virgin olive oil (EVOO), rich in antioxidant polyphenols, improves lipoprotein quality and reduces oxidative stress, which is emerging as a potential intervention in MPSH. This study aims to evaluate the impact of a high-cholesterol atherogenic diet (ATR) on maternal and fetal lipid profile, placental oxidative stress, and the expression of inflammation and cholesterol metabolism markers. Additionally, to determine if these effects could be reversed by EVOO supplementation.

Methods:
Pregnant C57BL/6 mice were divided into three groups: control (n=15), ATR diet (n=14), and ATR diet supplemented with EVOO (n=16). On gestational day 17.5, mice were euthanized, and samples were collected for lipid profile analysis in maternal serum, fetus, and placenta. Oxidative stress markers- MDA and superoxide were evaluated in the placenta using the TBARS assay and dihydroethidium (DHE) staining, respectively. Expression of cholesterol metabolism and inflammation genes were determined by quantitative PCR (qPCR). Ethical Committee of Universidad de los Andes approval (CEC2023035)

Results:
ATR diets showed altered maternal and fetal lipid profiles, increasing TC in both ($p<0.001$ and $p<0.05$, respectively) compared to the control group. Oxidative stress and inflammation markers in the placenta did not show significant changes. EVOO supplementation reduced fetal TC levels ($p<0.001$) and increased esterified cholesterol in the placenta ($p<0.05$) compared to the ATR group.

Conclusions:
The ATR diet induces a hypercholesterolemia model without significant inflammatory or oxidative stress alterations in the placenta. EVOO supplementation demonstrates a protective effect, particularly on cholesterol trafficking to the fetus, potentially mitigating the adverse effects of gestational hypercholesterolemia

Funding:
FONDECYT 1230527

Key-words: (up to 5):
hypercholesterolemia, Extra virgin olive oil, Cardiovascular risk

Abstract #00005484 en

Perspectives on the importance of parents' health and health-promoting behaviors during pregnancy on child health outcomes: a cross-sectional study

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Bijma Hilmar (1), Munshi Sushma (2), Bertens Loes (3), Weggelaar-Jansen Annemarie (4), Ernst-Smelt Hiske (3), Lambregtse-van den Berg Mijke (5), Harmsen van der Vliet-Torij Hanneke (6), Steegers Eric (7)
(1) Erasmus MC Department of Obstetics and Gynaecology, University of Humanistics , (2) Erasmus MC Department of Obstetrics and Gynaecology , (3) Erasmus MC, Department of Obstetrics and Gynaecology, (4) Tranzo, Tilburg University, (5) Erasmus MC Department of Psychiatry , (6) 5Rotterdam University of Applied Sciences, Research Centre Innovations in Care, (7) ErasmusMC Rotterdam, Department of Obstetrics and Gynaecology

Background/aims:
Adverse circumstances during pregnancy are associated with impaired health for children not only during pregnancy and childhood, but also in adulthood. Identification of adverse circumstances has important implication for the prevention of non-communicable diseases later in life. This study evaluates the perspectives of parents and professionals regarding the importance of parents' health, parents' health-promoting behaviour and psychosocial and lifestyle factors of parents during pregnancy on a child's long-term health outcomes.

Methods:
A cross-sectional survey study among parents with a child up to two years and professionals involved in preconception, pregnancy and childhood care in Rotterdam, the Netherlands. All parents with a child up to two years in Rotterdam were invited to participate. Professionals were included through medical and social organisations. We developed a questionnaire in co-creation with the target groups. Univariate, bivariate and multivariate analyses were done using SPSS.

Results:
1854 parents (response rate: 10.1%) and 322 professionals (response rate: 39.2%) participated. Most parents and professionals agree that maternal health during pregnancy is important for a child's health during pregnancy (98%, 99% respectively), childhood (94%, 97% respectively) and adulthood (84%, 89% respectively). Additionally, almost all parents and professionals agree that maternal health-promoting behaviour during preconception (90%, 96%, respectively), pregnancy (97%, 98%, respectively) and childhood (97%, 99%, respectively) is important for a child's health.

Conclusions:
Most parents and professionals recognize the importance of parents' health and well-being, parents' health-promoting behaviour and psychosocial and lifestyle factors of parents during pregnancy for a child's health throughout the life course. To optimize public health, there is a need for effective knowledge translation to bridge between recognition and health-promoting behaviour.

Funding:
This work was supported by The Dutch Organisation for knowledge and innovation in health, healthcare and well-being (ZonMw) [grant number 55400101].

Key-words: (up to 5):

Prevention, parental health and well-being, psychosocial and lifestyle factors, health-promoting behaviour

Abstract #00005485 en

Using Knowledge Graphs to understand child overweight and obesity risk for improved health decision-making and prevention

Big Data and Cohorts in DOHaD Research.

Massiris Miguel (1), Davidge Sandra (2), Goldowitz Daniel (3), Nepomnaschy Pablo (4), Wazana Ashley (5), Connor Kristin (6), Delrieux Claudio (1)

(1) Universidad Nacional del Sur, (2) University of Alberta, (3) University of British Columbia, (4) Simon Fraser University, (5) McGill University, (6) Carleton University

Background/aims:

Early biological, social, and environmental factors influence offspring development and risk for overweight/obesity throughout the lifecycle. However, our ability to use this evidence to predict health trajectories and prevent adverse outcomes is limited because information is often fragmented across diverse studies and databases. We hypothesized that using Natural Language Processing (NLP) and Knowledge Graphs (KGs) could improve the synthesis of fragmented evidence on early determinants of overweight/obesity, revealing established and novel exposure-disease relationships that could inform future prediction/prevention strategies.

Methods:

We conducted a literature review on childhood overweight/obesity (PubMed), compiling a sample database of 8,736 articles. Articles were processed using NLP algorithms to extract key data, including risk and resilience factors (classes). From these data, we created a KG, which is a way of organizing data as a network of interconnected entities and identifying the meaning of relationships between these entities. Next, we created a web-tool to capture relevant articles on child overweight/obesity using the KG. Users enter keywords, and the tool retrieves related papers using specific graph search algorithms. Last, we validated the effectiveness of our tool with 10 experts through a standardized usability scale (SUS) test, where an SUS score≧70/100 indicates good tool utility.

Results:

The KG comprised 15623 nodes (e.g. words) belonging to 58 distinct classes (e.g. diseases, exposures, interventions) and 232830 connections between nodes, distributed across five relationship types (Mentions/Author/Published_in/Co_ocurrence/Similar_to). Preliminary analysis (SUS=70/100) indicate fair usefulness of the tool, with room for improvement.

Conclusions:

We built a childhood overweight/obesity KG that captures relationships between risk and resilience factors, extracting and organizing these factors into a single network. This approach, with our user-friendly search tool, can synthesise fragmented scientific evidence, and help experts find relevant studies to understand early determinants of overweight/obesity. In the future, this tool could support decision-making for obesity prediction/prevention.

Funding:

Key-words: (up to 5):

Knowledge Graphs, Natural Language Processing, Obesity, DOHaD

Abstract #00005488 en

The role of continuity of care in building trust among parents and professionals during early life course: a qualitative study

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Bijma Hilmar (1), Munshi Sushma (2), Munshi Rachita (3), Weggelaar-Jansen Annemarie (4), Steegers Eric (5)
(1) Erasmus MC Department of Obstetrics and Gynaecology and University of Humanistics, (2) Erasmus MC Department of Obstetrics and Gynaecology , (3) Erasmus MC Department of Obstetrics and Gynaecology, Erasmus University, (4) Tranzo, Tilburg University, (5) ErasmusMC Department of Obstetrics and Gynaecology

Background/aims:
Trust is essential for effective integrated care, yet little is known how continuity of care contributes to building trust. Therefore, this study examines the role of continuity of care – relational, informational, and management continuity – in fostering interpersonal and institutional trust between (future) parents in vulnerable circumstances and professionals from the medical, social and public domain in the context of multi-domain integrated care during the early life course.

Methods:
This qualitative longitudinal study was conducted over a two-year period. In-depth, semi-structured interviews were carried out using purposive sampling with (future) parents in vulnerable circumstances and professionals from the medical, social, and public domain in Delfshaven, Rotterdam, The Netherlands. Thematic analysis, guided by a socio-ecological framework of trust, was conducted to identify key mechanisms through which continuity of care influences interpersonal and institutional trust.

Results:
We included 20 (future) parents and 22 professionals. Relational continuity strengthens interpersonal trust, with parents emphasizing the importance of having a single point of contact and professionals valuing openness about vulnerable circumstances with home visits being considered beneficial in this regard. Informational continuity is essential for institutional trust, with parents noting the burden of repeatedly sharing their stories and furthermore calling for more transparent data-sharing. Management continuity enhances institutional trust among professionals, with case coordinators and structured interprofessional collaboration improving care coordination and system efficiency.

Conclusions:
Strengthening continuity of care is essential for fostering interpersonal and institutional trust among (future) parents and professionals, which is crucial for establishing integrated care during the early life course.

Funding:
This work was supported by The Dutch Organisation for knowledge and innovation in health, healthcare and well-being (ZonMw) [grant number 55400101].

Key-words: (up to 5):
Continuity of care, early life course, interpersonal trust, institutional trust, integrated care

Abstract #00005491 en

The SPPIN Study: Social Media Strategies for Recruiting a Pregnant Cohort

Big Data and Cohorts in DOHaD Research.

Brar Simran (1), Wowdzia Jenna B (2), Weng Phoebe (1), Arcand Madelyn (1), Rameshwarsingh-Nowbutt Sapna (1), Ohanian Ruben (1), Ospina Maria B (1)
(1) Queen's University, (2) Women and Children's Health Research Institute, University of Alberta

Background/aims:
Online recruitment is becoming more common in pregnancy and birth cohort studies. However, there is limited empirical evidence on its cost-effectiveness, sample representativeness, and optimal advertising strategies. This abstract presents a preliminary evaluation of key performance indicators (KPIs) to measure the effectiveness and efficiency of social media campaigns for SPPIN (Society, Pregnancy, Postpartum & Infant Development), a pregnancy cohort study examining the relationships between social location, gut microbiota, maternal mental health, and infant neurodevelopment.

Methods:
The SPPIN study launched its social media campaigns in November 2024 using Instagram and Facebook as the two target platforms. Paid Instagram ads targeted individuals aged 18–49 located in Edmonton, Alberta, Canada. KPIs of reach, number of link clicks and average cost per click (CPC) were collected using Meta Business Ads Manager (Meta Platforms, Inc). We report overall campaign metrics and describe the top five best-performing campaigns based on link clicks and CPC. Highest- and lowest-performing campaigns by CPC were compared by ad type.

Results:
Of 75 participants recruited to date, 60% found the study through social media (n=34 [45.3%] using Instagram and n=11 [14.7%] via Facebook). Notably, Facebook contributed to recruitment without paid advertising. Fifty-one paid campaigns were posted on 98 Instagram (74 posters and 24 videos). The total reach was 141,574 users with 5,002 link clicks and at an average CPC of $0.53 CAD. The campaign with the most link clicks yielded 441 clicks, reaching 13,570 people, and costed $0.19 CAD per click. The most cost-effective campaign generated 425 clicks, reached 1,728 people, and costed $0.18 CAD per click.
Lowest-performing campaigns were long-form videos.

Conclusions:
Social media advertising is a valuable strategy for participant recruitment in longitudinal studies. Despite limited investment, Facebook contributed meaningfully and will be prioritized in future efforts. Campaign performance varied, with poster-type ads outperforming long-form videos in engagement.

Funding:
Canadian Institutes of Health Research (#487536) and Canada Research Chairs Program (CRC-2023-00153).

Key-words: (up to 5):
Pregnancy and birth cohort; recruitment strategy; social media

Abstract #00005494 en

Maternal immune response, maternal stress and CD81 expression in small extracellular vesicles are associated with infant growth outcomes

Mechanisms Determining Transgenerational Effects of Health and Disease

Rodrigues Gouveia Gisele (1), Camilo Caroline (1), Órdenes Amanda Noemí Vera (2), Rivera Pablo Valdebenito (2), Polanczyk Guilherme Vanoni (1), Martins Jr David Correa (3), Gutiérrez Jaime Agustín (2), Brentani Helena (1)
(1) Departamento & Instituto de Psiquiatria, Faculdade de Medicina FMUSP, Universidade de São Paulo, (2) Facultad de Ciencias, Universidad San Sebastián, (3) Center of Mathematics, Computation and Cognition, Federal University of ABC

Background/aims:
Maternal immune system balance pathogen defense with tolerance to the semi-allogeneic fetus during pregnancy. Insults like stress during this period lead to unfavorable fetal outcomes. Small extracellular vesicles (sEVs) mediate communication between maternal and fetal environments, playing a role in maintaining maternal tolerance. CD81, a protein found on sEVs, is involved in T and B-cell activation, and is associated with inflammatory diseases like pre-eclampsia. However, no studies have jointly assessed cytokines and the intensity of CD81 expression on sEVs in stressed pregnant women, and their relationship with fetal outcomes.

Methods:
Sample was selected from a Brazilian randomized clinical trial with primigravid adolescents in socially vulnerable conditions.This study was approved by the ethics committee. Maternal stress was assessed via childhood trauma and anxiety in the third trimester. Maternal cytokines and sEVs were measured by ELISA and size exclusion chromatography, respectively. CD81 expression was analyzed by Western Blot. Infant growth at 12 months was evaluated using WHO Child Growth Standards. Multiple linear regression tested maternal stress, cytokines, and CD81 as predictors of infant growth.

Results:
Maternal stress was associated with cytokine balance and CD81 expression. Evaluating these maternal variables in relation to infant growth outcomes, we found an association length/height-for-age z-score (zLEN) at 12 months. Although CD81 wasn´t individually significant, its removal caused the loss of model significance. The model remained significant after adjusting for potential confounders such as full-term births, maternal BMI, child's gender, and intervention group.

Conclusions:
Our findings suggest that changes in maternal cytokine balance in the third trimester and maternal stress are associated with the intensity of CD81 expression on EVs, and infant length/height at 12 months.

Funding:
FAPESP (#2018/18560-6, #2018/21934-5, #2016/22455-8, #2021/00607-9), CNPq (#310823/2021-8), and ANID #1221362

Key-words: (up to 5):
small extracellular vesicles; maternal cytokines; CD81 expression; infant length/heigh

Abstract #00005499 en

Food restriction during lactation increases basal blood glucose in adult male rats

Role of Infant and Young Child Feeding Practices on Long-Term Health

DIAS GINISLENE (1), DOS SANTOS PEREIRA CARLA LAIANDRA (2), ALBANEZ CARLOS EDUARDO (2), DOS SANTOS MARIA EDUARDA (2), MELLO GOMES RODRIGO (1), DE OLIVEIRA JÚLIO CEZAR (2)
(1) UNIVERSIDADE FEDERAL DE GOIÁS-UFG, (2) UNIVERSIDADE FEDERAL DO MATO GROSSO Campus SINOP-UFMT

Background/aims:
Early nutritional changes can predispose metabolic diseases appearance in later life. The aim of this study was to evaluate the long-term effect of maternal undernutrition during lactation on metabolic parameters, body composition, and glycemic homeostasis in male and female rat-offspring.

Methods:
Maternal food restriction (n=6 rats) was performed during the first 2/3 of lactation (only 50% of ad libitum feed offered to control dams (FR50 group). While the control (CONT group) was fed ad libitum. Body weight, food and water intake were measured every 2 days. At 90 days-old, the estrous cycle was assessed, and intraperitoneal glucose tolerance (ipGTT) and insulin (ipITT) tests were performed. At 100 days-old, the rats were exposed to cold (4 °C) for 12 hours, then euthanized to remove body tissue to quantify biometric parameters.

Results:
During experimental period, a 27.81% reduction in body weight was observed in CONT female rats compared to CONT males, and a 30% reduction in FR50 female rats compared to FR50 males ($P<0.001$). While food and water intake did not differ. Basal glycemia, was increased by 14.54% in FR50 male compared to CONT male rats ($P<0.001$), while in comparison to FR50 female, it was increased by 9.59% ($P<0.01$). Data from ipGTT and ipITT did not differ among groups. In relation to CONT male, CONT female rats had an 18.12% increase in the interscapular brown adipose (iBAT) tissue. In relation to CONT female, FR50 female had a 13.30% reduction in iBAT ($P<0.01$). In relation to CONT male rats, CONT female had an increase in mesenteric fat of 26.03% ($P<0.01$), while retroperitoneal fat and the extensor digitorum longus muscle did not differ.

Conclusions:
Malnutrition during lactation programs changes in glycemic homeostasis, predisposing offspring to glucose intolerance, a risk factor for diabetic condition.

Funding:
Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brazil (CAPES)

Key-words: (up to 5):
Food restriction; Lactation; Basal blood glucose; Metabolic programming.

Abstract #00005500 en

Longitudinal Analysis of Vaginal Microbiota in Brazilian Women During Pregnancy: Insights from the Araraquara Cohort

Mechanisms Determining Transgenerational Effects of Health and Disease

Pinheiro-Castro Natalia (1), Ramos-Silva Tamiris (1), Biagio Leonardo (1), Shirley Meghan (1), Fernandes Gabriel (2), Luzia Liania (1), Rondó Patrícia (1)
(1) University of São Paulo, (2) Fiocruz - Research Center Renê Rachou

Background/aims:
Brazil's unique ethnic and cultural diversity offers an opportunity to explore how maternal characteristics shape the vaginal microbiota during pregnancy. This study characterizes the vaginal microbiota of Brazilian pregnant women and its associations with demographic, socioeconomic, obstetric, nutritional and lifestyle factors in a prospective cohort.

Methods:
This is part of the Araraquara Cohort Study, which examined 100 healthy pregnant women in Araraquara, Brazil. Vaginal samples were collected at three gestational periods (12–17, 20–26, and 30–36 weeks) and analyzed by targeting the V3-V4 region of the 16S rRNA gene. Maternal characteristics were obtained through questionnaires. Alpha and beta diversity were assessed using Partitioning Around Medoids (PAM) analysis. Community State Types (CSTs) were identified based on the Jensen-Shannon Divergence matrix and PAM clustering; the optimal number of clusters was determined by the Calinski-Harabasz index. Differentially abundant taxa were identified using the Wald test from the DESeq2 package, with candidates selected based on Benjamini-Hochberg adjusted p-values (<0.05).

Results:
Alpha diversity indices (Shannon, Simpson, Chao) indicated low species diversity, consistent with Lactobacillus dominance. Diversity metrics remained stable across pregnancy periods, with no significant differences between women. Three CSTs were identified: CST-I dominated by Lactobacillus crispatus, CST-III by Lactobacillus iners, and CST-IV characterized by low Lactobacillus abundance. Initial associations between maternal variables and microbiota composition did not remain significant after adjustment for multiple comparisons. Stratification by maternal variables revealed no reproducible patterns throughout gestation.

Conclusions:
Although the microbial composition remained relatively stable during pregnancy, individual-level fluctuations highlighted the dynamic and transient nature of the vaginal microbiome. Despite the diversity observed in this population, no significant associations were found between maternal characteristics and vaginal microbiota, challenging the clinical relevance of microbiota profiling in healthy microbiota populations.

Funding:
São Paulo Research Foundation (FAPESP). Grant numbers: 2019/17318-0; 2015/03333-6; 2020/15365-8; 2023/02404-3; 2024/01014-0.

Key-words: (up to 5):
Lactobacillus, Microbiota, Pregnancy, Vagina

Abstract #00005509 en

Maternal high fat diet disrupts small intestinal metabolites and metabolic pathways differently across gestation

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Cardoso Lucas (1), Ferraz Thaina (1), Mohammadkhani Sadra (1), Bloise Enrrico (1), Connor Kristin (1) (1) Carleton University

Background/aims:
Gut metabolites are key modulators of nutrient absorption and immune defence. However, it is unclear which maternal gut metabolites are important for pregnancy health or fetal development, or how the maternal gut metabolome may be influenced by conditions like maternal obesity. We hypothesised that a maternal high fat (HF) diet would alter the maternal small intestinal (SI) metabolome in a manner that could influence pregnancy and offspring developmental trajectories.

Methods:
Female C57BL/6J mice were fed 60% HF or control (CON) diet six weeks before and throughout pregnancy. Maternal SI samples were collected at gestational day (GD) 12.5, 15.5 or 18.5. 635 metabolites were quantified in maternal SI (Clinical Biomarker 2.0MEGA assay; TMIC). Data were analysed using MetaboAnalyst 6.0 (false discovery rate adjusted q-value<0.05). Ethical considerations were met.

Results:
At GD12.5, levels of 17 metabolites were lower in HF SI vs. CON, including 3-hydroxyisobutyric acid (linked to metabolic disorders) and putrescine (key for epithelial barrier-function). Several metabolic pathways were enriched in HF SI vs. CON including: arginine and proline metabolism; glutathione metabolism; butanoate metabolism; citrate cycle; propanoate metabolism; and alanine, aspartate and glutamate metabolism. At GD15.5, pyruvic acid (key for cellular metabolism) levels were higher, and p-cresol sulfate (toxin) and HexCer(d18:2/24:0) (sphingolipid) were lower, in HF SI vs. CON. At GD 18.5, levels of three metabolites were lower, including propionic acid (short-chain fatty acid), and three were higher, including 3-hydroxybutyric acid (energy substrate for gut microbiota) in HF SI vs. CON. No metabolic pathways were enriched/diminished in HF SI vs. CON at GD15.5 or GD18.5.

Conclusions:
Maternal HF diet, especially in early gestation, alters SI metabolites related to cellular and bacterial energy metabolism, short-chain fatty acids, epithelial barrier-function, and several metabolic pathways. These changes could be indicative of compromised SI metabolism and gut microbiome, with subsequent negative influence on maternal health and fetal growth/development.

Funding:
Natural Sciences and Engineering Research Council of Canada

Key-words: (up to 5):
maternal health, small intestine, metabolome, obesity

Abstract #00005510 en

Difference in placental O-linked N-acetylglucosamine transferase (OGT) expression relation to tobacco use across the lifespan and during pregnancy

Mechanisms Determining Transgenerational Effects of Health and Disease

Camilo Caroline (2), Gouveia Gisele Rodrigues (2), Vieira Luana Martos (3), Euclydes Veronica (2), Polanczyk Guilherme Vanoni (2), Brentani Alexandra (3), Felipe-Silva Aloisio (4), Brentani Helena (2)

(2) Departamento & Instituto de Psiquiatria, Faculdade de Medicina FMUSP, Universidade de São Paulo, (3) Departamento de Pediatria, Faculdade de Medicina FMUSP, Universidade de São Paulo, (4) Hospital Universitário, Universidade de São Paulo, São Paulo

Background/aims:

Maternal smoking has a detrimental effect during pregnancy and leads to adverse gestational outcomes, including fetal growth restriction. O-linked N-acetylglucosamine transferase (OGT) is a key regulator of placental development, nutrient transport, and cellular stress response, also associated with malnutrition and fetal growth restriction. We investigated placental OGT protein expression and its relation with maternal tobacco consumption.

Methods:

Samples came from two randomized clinical trials (RCTs) (NTC02807818 and NCT04362098) and from the São Paulo Western Region Birth Cohort (ROC). This study was approved by the ethics committee. For RCT studies, tobacco use lifetime and during gestation were assessed via questionnaires. For the ROC cohort, tobacco use was assessed through a self-report of smoke during pregnancy. Immunohistochemistry (IHC) staining was performed to determine OGT protein expression (ab96718; Abcam). IHC slides were scanned and image analysis was conducted using the PPCV9 algorithm. Protein expression levels were calculated using the IHC Index formula. Student's t-test and Wilcoxon rank-sum test were used to compare the difference in OGT expression between use/non-use of tobacco.

Results:

We identified OGT expression in syncytiotrophoblasts, the transporting epithelium which mediates maternal-fetal exchange of nutrients. Tobacco-exposed groups exhibited increased OGT expression relative to non-exposed groups. A statistically significant difference in placental OGT levels was observed in relation to tobacco use for both RCTs and ROC samples (p-value <0.05).

Conclusions:

Our results suggest that both lifetime and pregnancy maternal smoking is associated with placental OGT expression levels. Given its crucial role in fetal nutrient delivery and metabolism, this may be an important biological pathway associated with fetal growth restriction observed in pregnant women with tobacco exposure, and future studies are needed to test this hypothesis.

Funding:

FAPESP (grants #2018/18560-6, #2018/21934-5, #2016/22455-8 and #2021/00607-9), CAPES (Finance Code 001), and CNPq (#310823/2021-8).

Key-words: (up to 5):

OGT; Placenta; Tobacco; Protein expression

Abstract #00005512 en

Climate-smart feeding strategies: integrating sugar beet in young goat nutrition to reduce long-Term CO_2 footprint in mediterranean region

Plant and Animal Health and Its Impact on Reproductive Age Individuals and Their Offspring

Abdennebi-Najar L (1), Penati M (2), Giráldez F.J (3), Ranilla M.J (4), De Matos L (2), Balbi O (2), Dehnavi M (3), Dadi Y (2), Salvi G (2), Cremonesi P (5), Biscarini F (5), Martin A (3), Ben Salem H (6), Ceciliani F (2), Andres S (3)
(1) UMR S938, CRSA St Antoine, INSERM, Paris, (2) Department of Veterinary and Animal Science, Università degli Studi di Milano, (3) Instituto de Ganadería de Montaña, CSIC-Universidad de León, (4) Departamento de Producción Animal, Universitad de León, (5) Istituto di Nazionale delle Ricerche, Lodi, (6) INRAT, Tunis

Background/aims:
The MEDGOAT project aims to mitigate livestock contributions to global warming in Mediterranean countries by (1) promoting goat farming and (2) integrating alternative local feed resources into feeding strategies to reduce CO2 footprint. Our study evaluates the potential of sugar beet as a partial maize substitute in the diet of fattening goat kids.

Methods:
Twenty-four young goats were divided into three groups (n=8 each) and fed isoenergetic pelleted diets containing 18% maize (control), 9% sugar beet, or 18% sugar beet. Key parameters analyzed include feed intake, metabolic response, microbiota composition in saliva, rumen, and feces, as well as methane reduction.

Results:
Replacing maize with sugar beet of the diet of kid goats does not affect their residual feed intake at older age. Notably, insulin levels significantly decreased in sugar beet-fed groups compared to controls which support a shift in carbohydrate metabolism. Rumen microbiota analysis revealed significant shifts in microbial diversity ($p < 0.05$), whereas fecal and salivary microbiota remained stable, suggesting that sugar beet inclusion influences ruminal fermentation and metabolic pathways.

Conclusions:
These findings contribute to sustainable feeding strategies that enhance animal health, resilience, and environmental sustainability in Mediterranean livestock systems.

Funding:
PRIMA-Section 2-Medgoat PROJECT- Horizon 2020

Key-words: (up to 5):
Climate, goat, feed supplements, Microbiome, Gaz emission

Abstract #00005522 en

Impact of Maternal Pre-Gestational High-Fat Diet and Different Types of Fatty Acid During Gestation and Lactation on Offspring Outcomes

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Nunes Ludmila (1), Alves de Souza Esther (1), Vales Mennitti Laís (2), Galutti de Castro Monteiro Débora (1), Pellegrini Pisani Luciana (1)
(1) UNIFESP, (2) University of Cambridge

Background/aims:
Within the DOHaD framework, pregnancy and lactation are critical developmental windows during which maternal nutrition exerts a profound influence on offspring health. Maternal obesity and excessive intake of saturated fatty acids (SFAs) are linked to increased metabolic risk, while polyunsaturated fatty acids (PUFAs) may confer protective effects. This study aimed to investigate the impact of maternal dietary lipid quantity and quality on anthropometric outcomes, adiposity, and activation of the TLR4 signalling pathway in white adipose tissue (WAT) of male and female offspring at 21 days of age.

Methods:
An experimental study was conducted using thirty female Wistar rats fed either a control (C) or high-fat (HF) diet during the pre-gestational period. During gestation and lactation, the animals were reassigned to different dietary groups based on fat content and source. The HF diet (4.6 kcal/g) consisted of 43% energy from lipids, primarily saturated fats (60% from butter). The normolipidic diets (3.9 kcal/g; 16% lipids) included different fat sources: soybean oil (n-6 PUFA), butter (SFA), and fish oil (n-3 PUFA). Maternal weight gain, offspring adiposity, and protein expression in WAT were assessed via Western blot.

Results:
Although maternal HF diet intake did not induce obesity, it impaired oral glucose tolerance. In male offspring at weaning, maternal HF diet led to increased visceral adiposity compared to those whose mothers received a normolipidic PUFA-enriched diet, and also relative to female offspring. Evaluation of the TLR4 signaling pathway in retroperitoneal WAT revealed no significant differences in protein expression among groups.

Conclusions:
These findings suggest that both the amount and type of dietary fatty acids during the perinatal period can influence metabolic outcomes in offspring, with PUFA-rich diets potentially mitigating adverse effects associated with maternal high-fat intake.

Funding:
São Paulo State Research Support Foundation (FAPESP) 2022/05529-9 and Coordination for the Improvement of Higher Education Personnel (CAPES) 88887.802376/2023-00)

Key-words: (up to 5):
DOHaD, maternal nutrition, fetal programming, offspring development, metabolic dysfunction

Abstract #00005525 en

Clinical and proteic biomarkers for predicting necrotizing enterocolitis and sepsis in preterm infants

Role of Infant and Young Child Feeding Practices on Long-Term Health

Hernández Martínez Alma Leticia (1), Dávalos Pérez Adriana (2), Ruíz Jaramillo Ma de la Cruz (3), Helguera Repetto Addy Cecilia (4), Irles Machuca Claudine Liliane (4), Lazo de la Vega Monrroy Maria Luisa (1), Barbosa Sabanero Gloria (1)

(1) Department of Medical Sciences, University of Guanajuato, (2) Department of Medicine and Nutrition, University of Guanajuato, (3) Hospital General León, Guanajuato, (4) "Isidro Espinosa de los Reyes", National Institute of Perinatology

Background/aims:

Necrotizing enterocolitis (NEC) is an ischemic and inflammatory bowel necrosis affecting preterm newborns after feeding begins. Neonates with NEC have high mortality rates and increased risk for long-term gastrointestinal and neurodevelopmental complications. During NEC, neutrophil extracellular traps (NETs) are formed to capture and eliminate pathogens, enzymes like elastase (ELA2) and cathepsin G (CatG) contribute by activating interleukin 33 (IL-33) to resolve intestinal hyperinflammation. Strategies are needed to predict necrotizing enterocolitis before the onset of clinical signs. Our aim was to evaluate ELA2, CatG, and IL-33 in umbilical cord plasma of preterm newborns and clinical data, in association with NEC and sepsis.

Methods:

This longitudinal study analyzed umbilical cord plasma from premature newborns: NEC (n=12), sepsis (n=27), and controls (n=41), and the perinatal clinical data. The study was approved by the corresponding research and ethics committees (CIBIUG-P50-2022, HGL-CIS-2022/073, PIHGL-CEIS-006-2023, INPer-2018-1-149). ELA2, CatG and IL-33 cord blood levels were quantified by ELISA. A $p < 0.05$ was statistically significant.

Results:

Gestational age ($p < 0.0001$), low weight ($p < 0.0001$), height ($p = 0.007$), caesarean section ($p < 0.0001$), type of pregnancy ($p = 0.004$), premature membrane rupture ($p = 0.007$), breast milk substitutes ($p = 0.050$), prolonged hospital stay ($p < 0.0001$), pregestational maternal weight ($p = 0.013$) high maternal cholesterol ($p = 0.015$) and triglycerides ($p = 0.030$) were associated with the development of NEC and sepsis. ELA2 cord levels at birth levels were found elevated and associated with the development of NEC and sepsis ($p < 0.0001$).

Conclusions:

ELA2, neonatal and maternal clinical variables were associated with the development of NEC and sepsis. More studies are needed to determine the value of ELA2, CatG and IL-33 as biomarkers of deterioration and progression of these diseases and neonatal outcomes.

Funding:

Frontier Science-CONACYT FORDECYT-PRONACES/116325/2020

Key-words: (up to 5):

Necrotizing enterocolitis, sepsis, ELA2, CatG, IL-33

Abstract #00005533 en

Gestational exposure to a high-fat diet conditions the ontogeny of hypothalamic nuclei that regulate eating behavior postnatally

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Galindo-Solano Rosa Nuria (1), Trejo-Villarreal Ximena (1), Díaz-Olivares Geovanna (1), Rea-Palomino Gustavo (1), Montes-Aguirre Dayna (1), Gutiérrez-Ospina Gabriel (1)
(1) UNAM

Background/aims:
The prevalence of pediatric obesity has risen over recent decades, likely due to inadequate feeding habits, poor food choices, and excessive infant intake encouraged by primary caregivers. Additionally, maternal dietary patterns before and during pregnancy may contribute to the morpho-functional conditioning of hypothalamic nuclei involved in postnatal regulation of eating behavior. To investigate this possibility, we fed female rats a high-fat diet (HFD) before and during pregnancy and examined fetal hypothalamic nuclei, assessing both neuronal size and density in regions implicated in postnatal eating regulation.

Methods:
Female Wistar rats were fed either a control diet or a high-fat diet (HFD) for 12 weeks. Obesity was confirmed in the HFD group before mating, after which both obese and control females were bred. Pregnant dams remained on their respective diets throughout gestation. At term, fetuses were collected, and their brains processed using immunohistochemical protocols. We then estimated and compared the density of orexin-positive neurons in lateral hypothalamus between fetuses exposed to HFD and those that were not.

Results:
HFD-fed mothers exhibited increased body weight, body length, Lee index, impaired glucose tolerance, and elevated serum triglyceride levels. These changes were accompanied by a marked reduction in reproductive efficiency and shifts in the offspring sex ratio. Litter size and the fetal sex distribution in uterine horns did not differ between control diet and HFD fed pregnant dams. Consistently, fetuses from HFD-fed mothers had lower body weight (14%). Additionally, the density of orexin-positive neurons increased across all hypothalamic nuclei in fetuses exposed to the HFD.

Conclusions:
Our findings indicate that fetal orexin-positive neurons in the lateral hypothalamus are already conditioned before birth by the gestational exposure to HFD. Whether this conditioning contributes to the rise in infantile obesity requires direct investigation.

Funding:
Programa Institucional de Obesidad y Diabetes del Instituto de Investigaciones Biomédicas, UNAM. Presupuesto anual otorgado por el IIB al laboratorio de Biología de Sistemas. Galindo-Solano, Nuria is a doctoral student from the Programa de Doctorado en Ciencias Biomédicas, Universidad Nacional Autónoma de México (UNAM) and has received CONAHCYT fellowship 748035.

Key-words: (up to 5): High-fat diet, gestational programming, hypothalamic development, orexin neurons and postnatal eating behavior.

Abstract #00005534 en

Maternal supplementation with fish oil, its effect on cerebral cortex development in rats fed a high-fat diet.

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Muñoz Carvajal Yasna (1), Montiel Juan (2), Kaune Heidy (2), Dagnino Alexies (3), Valenzuela Rodrigo (1), Toledo Jorge (1), Moraga Renato (1), Tabilo Luis (3), Flores Cristián (1), Maliqueo Manuel (1) (1) University of Chile, (2) Diego Portales University, (3) University of Valparaíso

Background/aims:
Supplementation with fish oil rich in n-3 fatty acids and especially docosahexaenoic acid (DHA) could ameliorate the deleterious effects of high fat diet (HFD) on offspring neurodevelopment. We next set out to test whether maternal supplementation with fish oil ameliorates the effects of HFD on the morphology of the cerebral cortex of the offspring during the postnatal period.

Methods:
Experimental model with Sprague-Dawley rats was used. Six rats with CD, 10% Kcal fat and 6 with HFD (45% Kcal fat). A subgroup of 5 HFD rats with 1% DHA fish oil supplement in the diet (HFD-FO).

Results:
In terms of cerebral cortex spine morphology, a higher quantification of “thin” spines was observed in males in HFD with compared to CD (P = 0.012; P = 0.002) and HFD-FO (P = 0.005). In females, an increase in first-order dendrites was observed in HFD relative to HFD-FO (P = 0.013) and fungi in DAG relative to CD (P = 0.014) and HFD-FO (P = 0.037). Relative to transcripts in males, increased Bdnf levels were observed in HFD-FO compared to CD and HFD in motor cortex (P = 0.019 and P = 0.016, respectively) and in auditory cortex in HFD compared to CD (P = 0.027), whereas in females, no significant results were observed. Moreover, n-3 PUFAs were higher compared to HFD in the auditory cortex in female offspring.

Conclusions:
Our results highlight the protective role of dietary n-3 PUFAs in counteracting the effects induced by HFD.

Funding:
Funding: Beca ANID N°: 211909311 / Operating Expenses of The Doctoral Thesis Project N° 24220033.

Key-words: (up to 5):
Obesity, n-3 fatty acids, DHA, cortex, neurodevelopment.

Abstract #00005535 en

Maternal high-fat diet disrupts the juvenile offspring's hippocampal synaptic plasticity and excitation/inhibition balance

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Cerna Camila (1), Ahumada Juan (2), Aguilar Freddy (1), Vidal Nicole (1), Rodríguez Guillermo (3), Thomas Samanta (4), Fuenzalida Marco (3)

(1) Universidad de Valparaíso, Programa de Doctorado en Ciencias Mención Neurociencias, (2) Universidad Andrés Bello, Millennium Nucleus of Neuroepigenetics and Plasticity (EpiNeuro), (3) Universidad de Valparaíso, Centro de Neurobiología y Fisiopatología Integrativa (CENFI), (4) Universidad de Valparaíso, Escuela de Nutrición y Dietética, Facultad de Farmacia

Background/aims:
Maternal nutrition during the perinatal period is critical in offspring development and long-term health. Beyond its established effects on metabolic and cardiovascular outcomes, increasing evidence highlights its influence on neurodevelopmental processes that sustain behavior and cognitive functions. Exposure to a maternal high-fat diet has been associated with cognitive impairments in offspring; however, the underlying neural mechanisms remain poorly understood. In this study, we hypothesized that cognitive deficits in offspring from high-fat diet-exposed dams are associated with changes in hippocampal synaptic plasticity and inhibitory transmission, processes fundamental to the proper functioning of neural circuits and cognitive performance.

Methods:
Female mice were fed a maternal high-fat diet (mHFD) containing 60% of calories from fat, starting one month before pregnancy and continuing throughout gestation until the end of lactation (Bioethics Approval CBC 26/2021). All experiments were conducted in the juvenile stage, between postnatal days 30 and 45. The offspring's memory was assessed using novel object recognition (NOR) and object location memory tests (OLM). Electrophysiological recordings were performed in the CA1 region of the hippocampus to evaluate the synaptic efficacy of pyramidal neurons.

Results:
Mothers exposed to a high-fat diet developed obesity, characterized by increased body weight and adiposity compared to control-fed dams. No significant metabolic alterations were detected in offspring. Despite this, mHFD offspring exhibited impaired cognitive performance, reflected by reduced discrimination indices in NOR and OLM memory tests. Electrophysiological analyses showed impaired hippocampal excitatory long-term potentiation and increased inhibitory synaptic efficacy, resulting in an excitatory/inhibitory imbalance.

Conclusions:
Maternal high-fat diet impairs hippocampus-dependent cognitive function in offspring. These deficits are associated with disrupted excitatory synaptic plasticity and enhanced inhibitory synaptic efficacy, leading to an excitatory/inhibitory imbalance. Synaptic dysfunction may be a key mechanism linking maternal obesity to neurodevelopmental alterations, highlighting the importance of maternal nutrition in shaping offspring brain function.

Funding:
ANID Fellowship 21202235, ANID-MILENIO NCN2023_032, ANID-FONDECYT 1241173, CIDI nº1 (CENFI-UV)

Key-words: (up to 5):

Maternal High-Fat Diel, Neuroscience, Memory, Synaptic Transmission

Abstract #00005536 en

Pannexin-1 overexpression is associated with neuronal loss in the prefrontal cortex of newborns gestated under chronic hypoxia

Impact of Early Life Exposures and Environmental Pollutants

Palma C. Daniel (1), Meza-Vilchez Osvaldo (1), Muñoz-Gusmán Fernanda (1), Orellana Luis (1), Borgoño S. Julian (1), Gonzalez-Candia Alejandro (1), A Herrera Emilio (2)
(1) Laboratory of Fetal Neuroprogramming, Institute of Health Sciences, University of O´Higgins., (2) Vascular Function & Reactivity Lab, Pathophysiology Program, ICBM, Universidad de Chile

Background/aims:
Gestational hypoxia can lead to fetal growth restriction (FGR). However, only a few studies have explored how FGR programs the perinatal brain. Previous precedents have shown that brain hypoxia is related to the opening of the Pannexin 1 (PANX1) channel, leading to cell death and inflammation. This study aims to demonstrate the effects of gestational hypoxia on the expression of PANX-1 channels and its relationship with neuronal density in the prefrontal cortex at two age stages: newborns and juveniles.

Methods:
This study was approved by the Institutional Bioethics Committee (certificate 20418-MED-UCH) and included four experimental groups, divided into two-time windows, normoxic (Nx1, n=5) and hypoxic neonates (Hx1, n=5) and normoxic (Nx75, n=5) and hypoxic juveniles (Hx75, n=5). All groups were introduced into a hypobaric chamber under conditions of normoxia (N, controls, 720 torrs, ~580 m) or hypoxia (H, 470 torrs, ~3800 m) during gestation until birth. Newborn and juvenile were euthanized, and the prefrontal cortex was collected to assess neuronal density, PANX1 expression, and cleaved Caspase 3. In addition, apoptosis was quantified using a TUNEL assay, ATP levels were measured using a fluorometric assay, and a nonparametric Student's t-test was used. Significant differences were considered when $p<0.05$.

Results:
Hypoxic gestations reduced neuronal density and increased TUNEL+ cells and caspase-3 protein levels in prefrontal cortex neurons. Finally, the immunopositive quantification of PANX1 in pyramidal neurons and total ATP increased in the prefrontal cortex of neonates and juveniles gestated under hypoxia compared to the normoxic group.

Conclusions:
Gestational hypoxia influences the expression of PANX1 channels, leading to an increase in cellular ATP levels and a subsequent reduction in neuronal density during both neonatal and juvenile stages. However, unexplored parameters within this field still require further in-depth investigation to comprehend their potential implications and underlying mechanisms fully.

Funding:
Fondecyt regular 1241626 **Key-words: (up to**

5):

Prenatal hypoxia, neuron, apoptosis, ion channels, DoHAD hypothesis.

Abstract #00005538 en

Impact of the form of birth, gestational age and effect of Flagellin on the activation of neonatal CD4+ T cells

Mechanisms Determining Transgenerational Effects of Health and Disease

Ventura Martinez Carlos Jesus (1), Kempis Calanis Linda Aimara (1), Santana Calderon Maria Angelica (1), Rodriguez Jorge Otoniel (1)
(1) Center for Research in Cellular Dynamics, UAEM

Background/aims:
Neonates represent a highly vulnerable population, accounting for over 40% of deaths in children under five, mainly due to infections. Neonatal T cells exhibit a Th2-biased response and distinct epigenetic landscapes, including reduced chromatin accessibility at Th1 gene loci like IFNG. Several factors, such as maternal nutrition, smoking, and delivery method, influence neonatal immune development. Studies show that cesarean-delivered neonates have a higher risk of developing childhood asthma and chronic inflammatory conditions later in life.

Methods:
Cord blood was collected from healthy full-term and preterm neonates, born via vaginal delivery or cesarean section at Hospital General Parres, with full informed consent and ethical approval (CONBIOÉTICA-17-CEI-001-20160329). Purified $CD4^+$ T cells or CBMC were stimulated using: 1) anti-CD3+anti-CD28, or 2) anti-CD3+Flagellin, based on evidence suggesting TLR5 signaling could provide co-stimulatory effects. We assessed homeostatic and stimulation-induced proliferation, activation of transcription factors (NFAT, NF-κB, AP-1), and production of key cytokines (IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-13, IL-17, IL-22, TNF-α, IFN-γ, TGF-β1), innate cytokines (IL-1β, IL-7, IL-8), and $CD8^+$ T cell effector mediators (Granzyme, Perforin), all measured by flow cytometry.

Results:
We observed differences in transcription factor activation and proliferation between T cells from neonates delivered vaginally or via cesarean section. T cells from cesarean births showed increased proliferation upon stimulation. Cytokine production patterns varied depending on the stimulation method. Notably, CD3+Flagellin stimulation enhanced proliferation in cells from both delivery groups, highlighting neonatal T cells' sensitivity to specific co-stimulatory signals.

Conclusions:
Birth method influences neonatal T cell responses, likely due to mechanical and hormonal changes during vaginal delivery that promote a tolerogenic program. In contrast, Flagellin stimulation suggests that TLR5 signaling may act as a co-stimulatory pathway in neonatal $CD4^+$ T cells.

Funding:
SECIHTI grants FC 1690 and CF 2019/1727995.

Key-words: (up to 5):
Neonates, T cells, TLR-5, C-section, Preterm.

Abstract #00005539 en

LONG-TERM EFFECTS OF OREGANO ESSENTIAL OIL SUPPLEMENTATION IN NEWBORN DAIRY CALVES

Plant and Animal Health and Its Impact on Reproductive Age Individuals and Their Offspring

Abdennebi-Najar L (1), Ceciliani F (2), Gini C (2), Gutiérrez-Expósito D (3), Arteche-Villasol N (3), Martin A (3), Cremonesi P (4), Fare F (5), Hosseini Ghaffari M (6), Javier Giráldez J (3), Andres S (3)
(1) UMR S 938, CRSA St Antoine, Inserm, (2) Department of Veterinary and Animal Science, Università degli Studi di Milano, (3) Instituto de Ganadería de Montaña, CSIC-Universidad de León, (4) Institute of Agricultural Biology and Biotechnology, Department of Bioinformatics, Biostatistics , (5) UNITECH OMICS platform, Università degli Studi di Milano , (6) Rheinische Friedrich-Wilhelms-Universität Bonn, Institute for Animal Science Physiology Unit

Background/aims:
We aimed to determine whether an early supplementation with EO in milk replacement improves shortand long-term growth, immunity microbiota, and metabolome in dairy calves.

Methods:
16 dairy calves were randomized to two groups. The C and treated (EO) group (providing 0.23 ml of oregano EO for 45 days). After weaning, calves were kept in a feedlot and fed ad libitum with a ration formulated to cover their nutritional requirements. The animals were weighed, and blood and fecal samples were collected on days 3 (T0), day 45 (T1), and day 370 (T2).

Results:
The EO group only had greater body weight and feed efficiency during the EO supplementation period. The CD14+ population average values were higher, whereas there was a lower abundance of Ruminococcaceae UCG-014, Faecalibacterium, Blautia, and Alloprevotella, and an increase of Allistipes and Akkermansia in the EO group. Some plasma metabolite changes, such as butyric acid, 3-indolepropionic acid, and succinic acid, particularly at T1, reflect parallel microbiota changes.

Conclusions:
An early EO supplementation increased feed efficiency during the suckling period and modulated the dairy calves' immunological systems with notable changes in microbiota and plasma metabolome. No significant effects were evidenced later for metabolome and microbiome except for the large abundance of several primary metabolites.

Funding:
PRIMA-SECTION 2-MILKQUA PROJECT 2018, HORIZON 2020

Key-words: (up to 5):
Cattle, Oregano, Nutrition, Immunity, Microbiome

Abstract #00005545 en

Cuban National Child Cohort Study (CNCCS): preliminary results of the relationships between birth weight and adult health

Big Data and Cohorts in DOHaD Research.

Vera Fernandez Yeneir (1)
(1) Lunenfeld Tanenbaum Research Institute

Background/aims:
The DOHaD theory that early life experiences can influence adult health still requires the contributions of new evidences from long-term prospective longitudinal studies. Cuba has a valuable database from the CNCCS which include information of all those born in the country during the first week of March 1973 (n = 4299) who were studied at birth, at 7 months and at 7, 11 and 17 years; now, as they reach their sixth decade of life, are being studied again.

Methods:
A questionnaire was administered to each participant covering sociodemographic data and current health conditions. In addition, a physical examination, anthropometric measurements, blood chemistry and carotid ultrasound were performed. These data were related to those obtained at birth and during childhood and adolescence but, in this work, only some current health data are presented (n=86): Body Mass Index (BMI), glomerular filtration rate (GFR), glycemia, cardiovascular risk, blood pressure and their relationships with birth weight.

Results:
Low birth weight participants showed higher systolic/diastolic blood pressure values (x
–
: 133,2±38,9/82,7±20,1 vs 122,8±13,9/79,2±10,0 mmHg) as well as cardiovascular risk (x
–
: 5,3 % vs 3,3 %), their GFR was also lower (x
–
: 80,0±13,6 vs 85,4±19,3 mL/min/1.73 m2). The relative risk of developing hypertension, elevated cardiovascular risk and abnormal glomerular filtration rate was also higher among people with a history of low birth weight.

Conclusions:
Although these results are preliminary and limited by the small number of people studied in the current follow-up, they corroborate the findings reported by other investigations. This research represents a unique opportunity to delve deeper into the patterns and mechanisms involved in DOHaD in the Cuban population **Funding:**

Lunenfeld-Tanenbaum-Research Institute Toronto-Canada and the Ministry of Health of Cuba.

Key-words: (up to 5):
Birth weight, hypertension, cardiovascular risk, glomerular filtration rate

Abstract #00005548 en

Gestational calorie restriction modulates hippocampal mitochondrial biomarkers in female wistar rat progeny

Mechanisms Determining Transgenerational Effects of Health and Disease

Ilha L (1), Stone V (1), Da Silvaa VF (1), Gindri-dos-Santos B (1), Maciel August P (1), Gayger-Dias V (1), Saraiva-Gonçalves CA (1), Matte C (1)
(1) Universidade Federal do Rio Grande do Sul

Background/aims:
Calorie restriction (CR) is a well-established intervention that promotes health and extends longevity in adult humans and animal models. However, the effects of CR during fetal development remain poorly understood. We previously showed that maternal calorie restriction prevents oxidative damage to hippocampal proteins, suggesting benefits related to redox state and mitochondrial health in offspring exposed to CR during gestation. This study aimed to investigate hippocampal markers of mitochondrial dynamics and key signaling pathways, specifically DRP1, mitofusins, NRF2, TFAM, sirtuins, PGC1-α, PI3K/Akt, and AMPK in offspring of female Wistar rats subjected to gestational CR.

Methods:
Wistar rat dams in the CR group received 20% less food compared to controls, with adjusted vitamin and mineral content to avoid undernutrition (n = 40). For Western blot analysis, one female pup per litter was selected (Ethics Committee #38809).

Results:
Maternal CR led to a decrease in the expression of TFAM [t(9)=3.291, p=0.0094] and DRP1 [t(10)=2.399, p=0.0374] in the hippocampus of female pups. No significant changes were observed in the expression of SIRT1 [nucleus: t(6)=0.001271, p=0.9990; cytoplasm: t(7)=1.183, p=0.2753], SIRT3 [t(10)=1.040e-010, p>0.9999], AMPK [t(9)=1.402, p=0.8916], Akt [t(10)=0.4041, p=0.6946], PGC1α [nucleus: t(6)=0.06823, p=0.9478; cytoplasm: t(7)=0.7805, p=0.4607], mitofusins [t(10)=0.1971, p=0.8477], or NRF2 [nucleus: t(5)=1.454, p=0.2058; cytoplasm: t(7)=1.195, p=0.2711].

Conclusions:
Maternal calorie restriction during gestation reduced TFAM and DRP1 expression in the offspring hippocampus, suggesting specific effects on mitochondrial biogenesis and dynamics.

Funding:
This work was supported by PROPESQ/UFRGS, FAPERGS (PQG 19/2551-0001747-2), CNPq (PQ2 303377/2021-6 and INCT 465671/2014-4), and CAPES.

Key-words: (up to 5):
Calorie restriction, Oxidative stress, Pregnancy, Hippocampus, DOHaD

Abstract #00005555 en

Gestational hypoxia-regulated Krüppel-like factor 4 via methylation of claudin 5 promotor is associated with increased blood-brain barrier permeability in the neonatal and juvenile prefrontal cortex

Impact of Early Life Exposures and Environmental Pollutants

Muñoz-Guzmán Fernanda B. (1), Meza-Vilches Osvaldo (1), Palma C. Daniel (1), Orellana Luis Octavio (1), Borgoño S. Julian (1), Herrera Emilio A. (2), González-Candia Alejandro (1)
(1) Laboratory of Fetal Neuroprogramming, Institute of Health Sciences, University of O'Higgins., (2) Vascular Function & Reactivity Lab, Pathophysiology Program, ICBM, Universidad de Chile

Background/aims:
Claudin 5 (CLDN5) is a transmembrane protein that constitutes a key component of tight junctions, playing a critical role in regulating the permeability of the blood-brain barrier (BBB). Krüppel-like factor 4 (KLF4) is an essential regulator of endothelial barrier function. We hypothesize that gestational hypoxia increases methylation in the promoter region of CLDN 5 binding to KLF4, decreasing its expression and increasing BBB permeability in newborns and the juvenile stage.

Methods:
All animal procedures were approved by the Institutional Bioethics Committee (certificate 20418-MED-UCH) and included four experimental groups, divided into two-time windows, normoxic (Nx1, n=5) and hypoxic neonates (Hx1, n=5) and normoxic (Nx75, n=5) and hypoxic juveniles (Hx75, n=5). All groups were introduced into a hypobaric chamber under conditions of normoxia (N, controls, 720 torrs, ~580 m) or hypoxia (H, 470 torrs, ~3800 m) during gestation until birth. Euthanasia was performed at birth (day 1) and in the juvenile stage (day 75) to collect brain tissue samples. CpG island methylation was assessed via pyrosequencing, while CLD5 gene expression was quantified using real-time PCR (qPCR), western blot, and immunohistochemistry (IHQ), and permeability is quantified by immunolocalization of perivascular albumin in prefrontal cortex tissue. A nonparametric Student's t-test was used. Significant differences were considered when $p<0.05$.

Results:
No changes in methylation profiles were observed in newborns. However, in the juvenile stage, transcript and protein levels of CLDN5 are decreased, which we associate with an increase in methylation profile and BBB permeability in the prefrontal cortex.

Conclusions:
Gestational hypoxia increased DNA methylation in CpG islands of the CLD5 promoter in juvenile guinea pigs, resulting in sustained downregulation of CLDN5 expression in the prefrontal cortex. This epigenetic alteration may compromise the long-term integrity of the BBB. However, the functional consequences of CLDN5 suppression during postnatal development remain to be elucidated in future studies.

Funding:
Fondecyt regular 1241626

Key-words: (up to 5):

Epigenetic programming, CpG, Neuroendothelial cells, Tight junction, Paracellular permeability

Abstract #00005560 en

Relationship between maternal factors and fetal growth velocity-FGV in pregnancies of women with HDP and GDM and healthy women.

Public Health Policies Across the Life Cycle.

Falcão de Carvalho Leticia (1), Alves Luzia Liania (2), Ramos Silva Tamiris (1), Domingos Biagio Leonardo (1), de Sousa Nobre Roseanne (3), Lana-Sales-Lacerda Jéssica (1), Pinheiro-Castro Natália (1), Rodrigues Batista Lívia Patrícia (1), de França da Silva Teles Laísla (1), Oliveira Aires Isabel (1), Lobo Marchioni Dirce (1), de Carvalho Rondo
Patrícia Helen (1)
(1) University of São Paulo, São Paulo, SP, Brazil, (2) Nutrition Department, School of Public Health, University of São Paulo, São Paulo, SP, Brazil, (3) Federal Institute of Education, Science, and Technology of Alagoas - IFAL,

Background/aims:
The DOHaD concept suggests that homeostasis affected during fetal development can influence body weight regulation and the occurrence of diseases in adulthood. Hypertensive disorders of pregnancy-HDP and gestational diabetes mellitus-GDM are the main maternal morbidities during this period and are directly related to fetal growth and unfavorable short and long terms outcomes. This study aims to evaluate the influence of maternal morbidity on FGV at three periods of pregnancy.

Methods:
This longitudinal study utilized data from the Araraquara Cohort Study (Ethics Committee-59787216.2.0000.5421) and selected 1,171 women with gestational age <18 weeks who were separated into three groups: 996 without morbidities, 45 HDP and 130 GDM and evaluated at three time points (<18, 20-29 and 30-39 weeks). Sociodemographic and lifestyle questionnaires were applied, and maternal anthropometric assessment and obstetric ultrasound were performed. Abdominal-AC and cranial circumference-HC, biparietal diameter-BPD and femur length-FL were measured in the fetuses. The values were transformed into Z-scores and FGV was calculated. Descriptive and bivariate analysis were performed, as well as the Generalized Estimating Equation-GEE to assess the effect of time and morbidity on fetal measurements.

Results:
Regarding FGV, only AC showed a significant difference between the groups (p=0.011) being higher in fetuses of mothers with GDM. Fetuses of smoking mothers had lower measurements for AC, HC and FL (p=0.036; 0.040 and 0.039 respectively). AC and BPD values were lower (p=0.001 and 0.021, respectively) in pregnant women with pre-gestational BMI below the IOM guidelines, and AC and BPD values were higher (p=0.018 and 0.028, respectively) for BMI above the recommended level. Lower values for AC (p=0.004) and FL (p=0.028) were observed in nulliparous and women under 19 years of age, respectively.

Conclusions:
Only GDM showed association with FGV of abdominal circumference, reaffirming the importance of public policies aimed at monitoring this metabolic disorder to identify changes throughout the gestational period.

Funding:
The São Paulo Research Foundation, FAPESP (2015/03333-6). Falcão de Carvalho, L received a PhD scholarship from National Council for Scientific and Technological Development, CNPq-Brazil.

Key-words: (up to 5):

Fetal Development; Gestational Diabetes; Gestational Hypertension; Biometry; Fetal Growth Velocity.

Abstract #00005567 en

DIABETES AND PREDIABETES IN POSTPARTUM RECLASSIFICATION OF GESTATIONAL DIABETES WOMEN. EDUGEST STUDY IN ARGENTINA

Big Data and Cohorts in DOHaD Research.

SALZBERG SUSANA (1)
(1) INSTITUTO CENTENARIO

Background/aims:
To describe the postpartum reclassification of glycemic status in a cohort of women with Gestational Diabetes (GDM) from the EDUGEST (Education in women with GDM) study, and to determine factors associated with a diagnosis of prediabetes or T2D.

Methods:
Methods: This observational and analytical study analyzed records of pregnant women with GDM recruited in the framework of the EDUGEST study. Data from QUALIDAB-GEST were analyzed for patients who completed postpartum reclassification at six weeks (as of May 2024). Information included concurrent cardiovascular risk factors, obstetric history in previous pregnancies, clinical and metabolic indicators, treatments, and postpartum reclassification results. Descriptive analyses were performed using means ± standard deviation (SD), medians with interquartile ranges [IQR] or proportions, as appropriate. Differences were tested using parametric and non-parametric tests. Regression models assessed factors associated with prediabetes or T2D development postpartum.

Results:
The analysis included 573 patients (median age: 31 [26-36] years; median gestational age at the first visit: 28 [26-32] weeks; BMI: 31.2 [26.7-34.9]). Postpartum reclassification showed 76.3% normal results, 19.5% prediabetes, and 4.2% T2D. The latter was significantly associated with insulin use during pregnancy (OR:
4.20) and family history of diabetes (OR: 3.21); while prediabetes was associated with hypertension (OR: 2.39), insulin use during pregnancy (OR: 1.62), BMI al the first visit (OR: 1.05), and fructosamine levels (OR: 1.01).

Conclusions:
This study identified locally relevant parameters associated with postpartum prediabetes and T2D in women with GDM, highlighting the importance of early identification of high-risk patients and the role of reclassification for timely diagnosis.

Funding:
World Diabetes Foundation

Key-words: (up to 5):
Gestational diabetes, Postpartum reclassification, Prediabetes, Type 2 diabetes

Abstract #00005569 en

L-Carnitine Modulates Ovarian Function and Follicular Reserve via Antioxidant and Steroidogenic Pathways

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Neira Melanie (1), Bordaquievich Mayra (1), Herrero Yamila (1), Velazquez Candela (1), Fritzler Analy Fernanda (2), Abramovich Dalhia (1), Parborell Fernanda (1)
(1) Instituto de Biología y Medicina Experimental (IBYME), (2) Hospital Dr. Pedro Fiorito

Background/aims:
Background: Carnitine is a vital nutrient involved in energy production and fatty acid metabolism. L-Carnitine (L-Car) also has antioxidant properties, potentially enhancing mitochondrial function. Due to its antioxidant effects, L-Car is being considered as a therapy for female infertility. It has been shown to improve reproductive health, promote oocyte health, and increase sex hormone and gonadotropin levels. However, the effect of L-Car on the female reproductive system, especially the ovaries, remains unclear. This study investigates L-Car effects on fertility and ovarian physiology in healthy female mice

Methods:
F1 mice (Balb/c x C57, 9 weeks, n=6/group) were injected IP with saline (control) or L-Car (200 mg/kg, five doses). Ovaries were collected on day
15 for histology (PSR staining), IHC for (DDX4, AMH, cleaved caspase-3, CD34, α-actin) and Western blot (CAT, SOD, BCL-2, BAX, VEGF, 3-βHSD, P450, STAR, Aromatase). Serum progesterone was measured by ELISA. Statistical analysis: T-test. (Ethics Committee #CE-007/2022)

Results:
L-Car treatment did not affect primordial follicle population but increased AMH expression ($p<0.05$). A decrease in apoptotic index in follicles was observed ($p < 0.05$). CAT and SOD levels were higher in the L-Car group, with no changes in PSR, BCL-2, or BAX.No significant effect of L-car on ovarian angiogenesis was observed. STAR and aromatase were upregulated by L-car, while other steroidogenic markers remained unchanged.

Conclusions:
The results suggest that L-car has a modulatory effect on ovarian function, with a focus on follicular preservation and the regulation of steroid synthesis. However, it would not affect angiogenesis or the levels of certain key biomarkers related to apoptosis and steroidogenesis.

Funding:
ANPYCT, CONICET, Fundación Williams, Fundación René Barón, Fundación IBYME

Key-words: (up to 5):
Ovary, L-carnitine, antioxidant, steroidogenesis, ovarian physiology.

Abstract #00005574 en

Neonatal neglect increases the risk of the cardiometabolic disorder in adulthood: a pre-clinical model

Mechanisms Determining Transgenerational Effects of Health and Disease

Palafox-Sánchez Victoria (1), Maldonado-Ruíz Roger (1), Guajardo-Correa Emanuel Adrían (1), Luevano-Martínez Luis Alberto (1), López-Morán Silvia Araceli (1), Bernal-Ramírez Judith (1), Chapoy-Villanueva Hector (1), Pérez Manuel (2), Lozano-García Omar (1), García-Rivas Gerardo (1)
(1) Institute for Obesity Research, Tecnológico de Monterrey, Monterrey, México, (2) Escuela de medicina y Ciencias de la Salud, Centro de Primera infancia, Tecnológico de Monterrey

Background/aims:
Adverse childhood experiences (ACEs), such as neglect and physical or sexual abuse, are potentially traumatic events that occur during childhood and can have long-lasting effects on physiological function into adulthood. ACEs are known risk factors for developing obesity, cardiovascular disease, and depression; however, they remain underrecognized in cardiometabolic clinical practice. This project evaluated the effect of maternal separation as a model of neglect neonatal (NN) on the cardio-metabolic phenotype in mice, using a combined model of NN and hypertensive-obesity in adulthood.

Methods:
All animal procedures were approved by the Tec de Monterrey-CICUAL. C57BL/6 male and female mice (8 weeks old) were used for breeding. The offspring male and female pups-underwent maternal separation (postnatal days 2-21, 3h/day). At 10 weeks old, mice were fed either a standard chow or high-fat diet (HFD) and HFD groups received L-NAME supplemented drinking water for 12 weeks. Mice were assigned to one of four experimental groups: 1.Control+Chow, 2.Control+HFD, 3.NN+Chow, 4.NN+HFD.

Results:
Weekly weight gain was significantly higher in male mice in the NN+HFD group compared to the Control+HFD from week 6 onward. In contrast female mice did not exhibit this effect. Additionally, male mice in the NN+HFD-group showed increased body fat percentage and hepatic steatosis compared to the Control+HFD group. Cardiac function was assessed by echocardiography. Systolic function parameters remained unchanged in both male and female mice across diets; however, diastolic function was impaired exclusively in male NN+HFD group, as evidenced by alterations in deceleration time, isovolumic relaxation time and the E/A ratio. Signs of hypertrophy, pathological remodeling and mitochondria alterations in the left ventricle showed a trend toward an increase in male mice in the NN+HFD group vs Control groups.

Conclusions:
These results suggest that the male mice exposed to early-life stress through neonatal neglect experience exacerbated cardio-metabolic alterations in adulthood when subjected to hypertensive-obesity model.

Funding:
CBR 2022. Fondo semilla 2024-Centro Primera Infancia

Key-words: (up to 5):
Adverse Childhood Experiences (ACEs), Neglect, Maternal Separation, Cardiometabolic disease

Abstract #00005575 en

Effects of gestational ethanol exposure on epigenetic reprogramming in blood-brain barrier cells

Impact of Early Life Exposures and Environmental Pollutants

Barros Matheus (1), Stipursky Joice (1)
(1) Institute of Biomedical Sciences, Federal University of Rio de Janeiro

Background/aims:
Alcohol consumption during pregnancy is a major cause of global developmental deficits, resulting in long-term sequelae and characterizing Fetal Alcohol Spectrum Disorder (FASD). This disorder can impair neurodevelopment, leading to deficits in memory, attention, learning, and underdevelopment of brain regions such as the corpus callosum, hippocampus, and cerebral cortex. Prenatal ethanol exposure may affect the blood-brain barrier (BBB), composed of endothelial cells (ECs), astrocytes, and pericytes, which supplies nutrients and oxygen to the central nervous system (CNS) and protects it from neurotoxic substances. Recent evidence indicates that ethanol can cause epigenetic dysregulation, altering the expression of genes essential for neurodevelopment. Our group previously showed that ethanol-exposed ECs exhibit reduced expression of tight junction proteins (ZO-1), the glucose transporter (GLUT-1), and altered secretion of angiogenic proteins. In this study, we investigated whether these dysfunctions could be linked to changes in the DNA methylation profile of ECs.

Methods:
A murine model was used, with gestational ethanol exposure (3 g/kg at 30%) via daily gavage from gestational day 14 to 19 (Ethics Committee 038/24). After birth, the cerebral cortex of neonates was collected for the isolation of murine brain endothelial cells (MBECs) for culture or fixed for immunohistochemical analysis.

Results:
Culture purity was confirmed by >80% PECAM-positive cells. Immunofluorescence for 5-methylcytosine (5mC) revealed a 38% reduction in DNA methylation in MBECs from ethanol-exposed animals compared to controls. In parallel, HBMEC (human brain microcapillary endothelial cells) lines exposed to 50 mM and 100 mM ethanol also showed reduced 5mC labeling, which was reversed by treatment with S-adenosylmethionine (SAM, 50 µM).

Conclusions:
These results demonstrate the successful isolation of MBECs and suggest that prenatal ethanol exposure alters DNA methylation profiles, potentially reversible by SAM. Future steps include analyzing endothelial functional genes expression via RT-qPCR and performing functional assays to assess the impact of DNA hypomethylation on EC function.

Funding:
CAPES

Key-words: (up to 5):
FASD, ethanol, neurodevelopment, blood-brain barrier (BBB), methylation

Abstract #00005581 en

Early life conditions and neurocognitive development: protocol of a prospective cohort study in Cuban adolescents

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Vera Fernandez Yeneir (1), Esquivel Mercedes (2), Estevez Nancy (3), Machado Maria del Carmen (4), Ruben Mercedes (5), Tamayo Vilma (6), Rancel Mayda (7)
(1) Alliance for Human Development, Lunenfeld Tanenbaum Research Institute, (2) Research Group of Human Growth and Development, University of Medical Sciences of Havana, (3) Cuban Neurosciences Centre, (4) Cuban Neuroscience Centre, (5) Victoria de Girón Faculty of Medical Sciences, (6) Research Group of Human Growth and
Development,University of Medical Sciences of Havana, (7) Research Group of Human Growth and Development, University of Medical Sciences of Havana, Cuba

Background/aims:

The influence of early life conditions on the genesis of a range of non-communicable diseases is widely accepted, but their impact on children's neurocognitive development is less well known. Many studies are based on retrospective data and there is little prospective research about the associations of factors such as maternal nutritional status or stress during pregnancy with neurodevelopment during childhood and adolescence. This study aims to examine whether prenatal, perinatal and postnatal conditions are associated with brain and neurocognitive development in a cohort of Cuban adolescents.

Methods:

The cohort includes 341 mother-child pairs residing in Havana who were recruited at birth from January to June 2016 and followed monthly until 6 months of age. Prenatal, perinatal, and postnatal variables were studied, including maternal health, nutritional and psycho-emotional status, infant health, growth, and a set of sociodemographic variables. The new follow-up includes the collection of sociodemographic data as well as assessments of adolescent health, anthropometric measurements, neurocognitive development (intellectual capacity, executive functions, academic performance), anxiety, depression and anatomical, functional and near infrared spectrometry resonance images for the evaluation of brain anatomical development with the aim to identifying the variables that explain brain and neurocognitive development as well as the health situation of adolescents controlling the effect of biological, sociodemographic and psychological covariates. Univariate and multivariate techniques will be used to identify which variables among those studied contribute to a significant independent risk of the presence of deviations in neurocognitive development and /or health status in the adolescents studied.

Results:

Conclusions:

The study has been approved by the Health Research Ethics Committee of the Julio Trigo López School of Medical Sciences, and its findings will be presented at national and international conferences and publications.

Funding:
Alliance for Human Development-Lunenfeld Tanenbaum Research Institute and Cuban Neuroscience Centre (Common Funds for Cuban Research Projects) **Key-words: (up to 5):**

Birth weight, neurodevelopment, growth, health status

Abstract #00005582 en

In vitro study of the effect of serum from hypothyroxinemic mice on lipid accumulation in 3T3-L1 cells.

Mechanisms Determining Transgenerational Effects of Health and Disease

Gallegos Andrés (1), Millaleo Bárbara (2), Regaldiz Alejandro (3), Santos Jhoana (3), Riedel Claudia (3), Bohmwald Karen (4), Vechiolla Andrea (5), Opazo Ma. Cecilia (2)
(1) Universidad de las Americas, (2) Universidad de las Américas , (3) Universidad Andres Bello, (4) Universidad Autonoma, (5) Pontificia Universidad católica de chile

Background/aims:
Maternal hypothyroxinemia (HTX) has been linked to large-for-gestational-age (LGA) offspring, who often experience adiposity, metabolic syndrome, and obesity. Initial observations showed that adult mice exposed to HTX developed an LGA phenotype with increased body fat and adipocyte hypertrophy. Here, in vitro study using 3T3-L1 cells investigated the mechanisms behind this hypertrophy aiming to explore the effects of HTX mouse serum on adipogenesis, lipid accumulation, and gene expression related to lipogenesis and adipogenesis in 3T3-L1 cells, using murine serum instead of the standard bovine serum to assess the impact on adipocyte development and gene expression.

Methods:
In this study, we induced HTX in mice by administering MMI in their drinking water for 14 days. Serum was collected from the HTX-treated and a control group (n=10) under the bioethics committee (UNAB/N°005/2022) regulations. The serum from the HTX-treated mice was then used to induce adipogenesis in 3T3-L1 cells. Oil Red O and Nile Red staining assessed lipid accumulation. Furthermore, the expression of key genes related to lipid accumulation, specifically PLIN1, mTOR, SREBP1c, and GLUT4, was analyzed using real-time PCR.

Results:
The obtained results showed a significant increase in lipid accumulation in the HTX group, observed as a higher number of lipid droplets per cell and an increased Nile Red fluorescence intensity compared to the control serum group. Additionally, mTOR expression was decreased, which is associated with increased lipid accumulation, while SREBP1c expression, a proadipogenic factor, significantly increased.

Conclusions:
The increase in lipid accumulation in 3T3-L1 cells and the alteration of key adipogenic genes expression associated with adipose tissue hypertrophy contribute to explain the LGA phenotype observed in HTX mice.

Funding:
UNAB DI-02-21/APP, UDLA DI-08/22,IMII PROGRAMA ICM - ANID, ICN09_016. FONDECYT 11221280, Centro de Investigación en Ciencias Biológicas y Químicas (UDLA).

Key-words: (up to 5):
Hypothyroxinemia, LGA, Adipocyte, Adipogenesis, Lipid accumulation.

Abstract #00005584 en

IMPROVING DIETARY PATTERNS AND REDUCING ULTRA-PROCESSED FOOD INTAKE IN GESTATIONAL DIABETES: FINDINGS FROM THE EDUGEST STUDY

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

sosa evangelina (1)
(1) Centro privado de endocrinologia

Background/aims:
Dietary planning, therapeutic education, and physical activity are key pillars for achieving glycemic control in women with Gestational Diabetes (GDM). Ultra-processed food (UPF) consumption increased prevalence of obesity and type 2 diabetes, due to high levels of added sugars, saturated fats, sodium, and additives, which raise energy intake and displace nutritious food, making intervention during pregnancy especially critical. Aim: to evaluate nutritional interventions from GDM diagnosis to postpartum, analyzing dietary patterns, by level of food processing and nutrient intake, before and after educational strategies.

Methods:
Multicenter quasi-experimental study on 914 women with GDM with a mean age of 30.8±6.3 years, 35.8% with obesity and Gestational age of 28.3±5.5 weeks at the first visit. A structured and multidisciplinary education program was developed to improve dietary habits. GDM diagnosis was based on the ALAD/NICE criteria, and nutritional and clinical parameters were assessed before and after the intervention. Dietary data were obtained using NutriQuid-Gest, a validated, structured, and self-administered questionnaire developed for this study. To analyze dietary patterns according to the level of food processing, the NOVA classification system was applied. For descriptive analysis, mean ± standard deviation (SD) were used due to the normal distribution of the variables. Student's t-test was used for comparisons between continuous variables.A significance level of $p \leq 0.05$was considered. All ethical and human welfare considerationshave been respected.

Results:
Most indicators improved significantly post intervention. A significant reduction in the consumption of ultra-processed foods and an increase in unprocessed or minimally processed foods was observed.
Ultra-processed foods (portion) pre 12.8±10.3 vs6.1±5.2($p < 0.000$). Newborn weight x3.2±0.5kg.

Conclusions:
Changes in dietary habits can be achieved through educational intervention, reducing UPF consumption and its associated risks, and lowering the likelihood of GDM-related complications. Nutritional intervention with an educational approach improves eating habits and should be prioritized as first-line therapy in GDM.

Funding:
WORLD DIABETES FUNDATION

Key-words: (up to 5):
Gestational diabetes-ultra-processed foods-education.

Abstract #00005595 en

Life cycle health: birth conditions, lifestyle habits and adult well-being Cohort Study

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Cardoso Viviane (1), Gratão Otávio (1), Padilha Luana (2), Ribeiro Cecília (2), Grandi Carlos (3), Carmona Fabio (1),
Rocha Paulo (1)
(1) Ribeirão Preto Medical School, University of São Paulo, (2) Department of Public Health, Federal University of Maranhão, (3) Research Committee, Argentine Society of Pediatrics

Background/aims:
The impact of early life conditions on outcomes throughout the life cycle is already known, however, there are still methodological challenges to be overcome. This study aims to investigate the direct and indirect effects of sociodemographic and economic factors at birth, maternal characteristics, and birth phenotypes on lifestyle, well-being, and nutritional status in adulthood within a Brazilian birth cohort.

Methods:
Data were analyzed from a birth cohort of 1978/79 in Ribeirão Preto, São Paulo. Independent variables were obtained through a questionnaire on sociodemographic and economic factors at birth and maternal characteristics. According to Williams birth phenotypes were defined as small and large for gestational age (SGA, LGA). Dependent variables were collected in 2016/17, when 1742 participants were between 37 and 39 years old. At that time, information on sociodemographic and economic factors, lifestyle, well-being and nutritional status was obtained. For data analysis, confirmatory factor analysis and structural equation modeling were used to identify latent variables and analyze association pathways. Ethical approval was granted by the Research Ethics Committee of the Hospital das Clínicas, FMRP-USP (CAAE 45485915.7.0000.5440).

Results:
Socioeconomic status at birth and in adulthood had a direct positive effect on lifestyle [standardized coefficient (SC) 0.668] and well-being (SC 0.565). Maternal smoking, on the other hand, had a negative effect on these outcomes (SC -0.202 and -0.149). Regarding birth phenotypes, individuals classified as LGA had a positive effect on well-being (SC 0.202), while those classified as SGA showed no direct effect on this outcome. Additionally, neither SGA nor LGA had direct effects on lifestyle.

Conclusions:
Birth phenotypes did not represent risk factors for lifestyle and well-being in adulthood. Furthermore, the findings highlight the importance of a favorable socioeconomic condition both early in life and in adulthood for adopting a healthy lifestyle and promoting well-being.

Funding:
This research was supported by CNPq and DECIT CNPq (Proc. Nº 400943/2013-1).

Key-words: (up to 5):
Lifestyle, Psychological Well-being, Child Health, Birth Cohort, Social Class

Abstract #00005598 en

MORPHOLOGICAL, MORPHOMETRIC AND MOLECULAR CHARACTERISTICS OF THE HUMAN PLACENTA DEPENDING ON PSYCHO-SOCIAL FACTORS.

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

ESTRADA JUSSELIT (1), del Sol Calderón Mariano (2), González Marcelo (3), Miglino María Angélica (4)
(1) Universidad de la Frontera y Universidad San Sebastián , (2) Universidad de la Frontera, (3) Universidad de Concepción, (4) Universidad de Unimar

Background/aims:
To link capillary cortisol in pregnant women with the morphological, morphometric and molecular characteristics of the total placenta villus, the fetus blood capillaries and the psycho-social factors of the pregnant woman.

Methods:
Cohort study shows 114 pregnant women. Inclusion criteria were: over 18 years old, without chronical cardiovascular diseases, early registering in the prenatal control. Those women presenting Cushing syndrome, erythematosus lupus and rheumatoid arthritis were excluded. The protocol was approved by the Ethic Committee belonging to the Health Service of Concepción. The Psycho-social Risk Score, the Edinburgh Score and the Life-long Violence Questionnaire were applied. Cortisol was measured through hair extraction. After delivery, placentas were analyzed by weighing their thickness, diameter, area and cotyledons. The characteristics of the umbilical cord were also analyzed.

Results:
To date, 114 pregnant women have been included and 58 have given birth: 41% vaginal delivery and 59% cesarean. Psycho-social risk was presented by 70%; 25% presented depression symptoms. Regarding violence records, 47.8% reported psychological violence, 35.1% physical violence and 40.4 % reported sexual violence. The average placenta weight was 508.6 g, with an area of 30.538.46 mm^3, thickness 19 mm and 18 cotyledons in average. The central insertion of the cord predominated. One placenta presented velamentous insertion, showing veins of 10 mm in diameter inserted in the amniotic membranes. An abnormality, succenturiate lobe placenta, was observed. It was characterized by a 16x15 mm lobule and by another 13x8 mm lobule, connected to the main placenta by blood vessels.

Conclusions:
The pregnant women present high levels of depressive symptomatology and psycho-social risk factors, which may influence over the placenta characteristics. There is still little evidence to prove this hypothesis. The other results will be ready before the congress.

Funding:
Research fellow ANID-Chile

Key-words: (up to 5):
placenta, morphology, depressive disorder, anxiety, chronical stress.

Abstract #00005599 en

Biopsychosocial factors during pregnancy and their influence over the autism spectrum.

Mechanisms Determining Transgenerational Effects of Health and Disease

ESTRADA JUSSELIT (1), Aguayo Ana Sol (2), Garrido Javiera (2), Neira Ivonne (2), Nova Daniela (2), Parra Sofia (2) (1) Universidad de la Frontera y Universidad San Sebastián , (2) Universidad San Sebastián

Background/aims:
Gestation is a sensitive phase influencing the development and wellbeing during adulthood. Etiology of the Autism Spectrum Condition (ASC) has been determined as coming from environmental factors. This condition is characterized by persistent difficulties in behavior, socialization, interaction and communication. It has been increasing, and now 1 in every 160 children in the world presents it. The objective was to determine the biopsychosocial risk factors present during pregnancy and associated with ASC.

Methods:
Systematic revision between 2013 and 2024 of the data bases PubMed, Scielo, WoS, Science, Lilacs and Scopus, identifying 24 papers fulfilling the criteria of inclusion and exclusion. Variables were determined using mnemonics PIO, with the words: gestation, risk factors and autism spectrum condition. Key and free expressions were included. Each set was bonded to the Boolean operator OR. The search was limited by using the Boolean operator AND.

Results:
Within the psychological factors, it has been proved that there is a relationship between the mothers' mental health and the development of the Autism Spectrum Condition in their descendants, independently from whether they are under treatment or not. Regarding biological aspects, factors showing a significant association with the development of the disorder were identified: mother's age, premature delivery, cesarean, complications during gestation and the masculine gender of the fetus. Cortisol levels are related to increase in the symptomatology of the disorder; they are more prevailing in the masculine gender. Regarding social conditions, some were identified; although no significant association with ASC development was found.

Conclusions:
The detection and treatment of conditions and pathologies associated with fetal programming related to ASC not only appear as fundamental, they must also be included within the pre-conception and prenatal care. Further research is also needed.

Funding:

Key-words: (up to 5):
Autism spectrum, fetal programming, Biological factor, Social factor, Psychological factor.

Abstract #00005602 en

Effects of food consumption pattern on nutritional status in childhood

Role of Infant and Young Child Feeding Practices on Long-Term Health

Herrera Guadalupe (1), Severi Cecilia (2), de Vasconcellos Carvalhaes de Oliveira Raquel de Vasconcellos Carvalhaes de Oliveira (3)
(1) Universidad de la República , (2) Universidad de la República, Uruguay, (3) Fundacao Oswaldo Cruz

Background/aims:
Nutritional habits acquired in childhood are linked to future habits. Ultra-processed products are increasingly occupying a place in the food consumption patterns of populations and are also one of the factors related to the development of overweight and obesity. In Uruguay, the importance of ultra-processed products in consumption patterns is increasing, both in adults and children. The aim of this study was to evaluate food consumption patterns and their effects on nutritional status in two waves of a cohort of children from Uruguay.

Methods:
Analytical cross-sectional study based on the analysis of the Nutrition, Child Development and Health Survey. Children from urban areas aged 24 to 47 months are included. The dietary patterns were constructed through cluster analysis using a nonhierarchical method of the Partitioning Around Medoids algorithm and its effects on the nutritional status were estimated by multinomial logistic models. 3 to 5 consumption patterns were constructed, always identifying the existence of a healthier pattern and patterns with a greater weight of ultra-processed products.

Results:
A significant effect of the consumption pattern was found in the first wave, increasing overweight and obesity and generating an increase of more than 10 percentage points with a positive interaction effect between the consumption patterns of both waves.

Conclusions:
Consumption patterns in the first years of life begin to show their impact even before school age.

Funding:
No funding was received for this study

Key-words: (up to 5):
nutritional status, food consumption, processed foods, preschool

Abstract #0000 4782
en

Building the Foundations for Early-Life Exposome Research based on the Chilean CHiESS Framework: preliminary data integration results.

Impact of Early Life Exposures and Environmental Pollutants

Urquidi Cinthya (1), Sepúlveda-Peñaloza Alejandro (1), Matus Patricia (1)
(1) Universidad de los Andes

Background/aims:
The double burden of diseases and the accelerated epidemiological transition in Latin America demand innovative frameworks to understand early-life determinants of noncommunicable diseases. In Chile, we developed the Chilean Exposome-Based System for Ecosystems (CHiESS), a technological and conceptual platform integrating multilevel environmental, clinical, and omics data, grounded in the One Health approach. In this abstract, we present an adaptation of the CHiESS framework for investigating childhood obesity by defining early-life exposure levels and sensitive windows, and integrating environmental and social data to identify vulnerability hotspots across Chile.

Methods:
Using CHiESS, we defined early-life exposure levels across critical developmental windows, operationalized through a nested structure based on the communal administrative division. A secondary analysis was conducted by integrating environmental exposure indicators from national surveys and social determinants data from the Longitudinal Survey of Early Childhood (Encuesta Longitudinal de la Primera Infancia, ELPI). Harmonized indicators were geospatially analyzed to construct cumulative exposure profiles at the communal level.

Results:
The adapted CHiESS conceptual framework for childhood obesity research operationalizes environmental and social exposures across four nested levels—ecosystem, community, population, and individual—centered on the commune as the primary spatial unit. Preliminary results show the successful integration of national environmental (pollutants) and social datasets for a historical cohort of 7,540 mother-child dyads, with children born between 2006 and 2008. This integration enabled the identification and geospatial mapping of vulnerability hotspots for childhood obesity across all Chilean communes. Exposures were mapped according to critical sensitive windows, including prenatal development and early childhood (from birth to 5 years of age). This integration enabled a preliminary identification and geospatial mapping of vulnerability hotspots for childhood obesity across all Chilean communes.

Conclusions:
Our preliminary secondary data integration and the adapted conceptual framework demonstrate the potential of exposome platforms and hotspot-based strategies to advance early-life preventive public health policies.

Funding:
Key-words: (up to 5):
childhood obesity, exposome, early environmental exposures

Abstract #00005604 en

Risk patterns and perinatal variables as predictors of cardiovascular damage in Uruguayan adolescents

Mechanisms Determining Transgenerational Effects of Health and Disease

Alfonso Daniela (1), Caetano Prates Enirtes (2), Severi Cecilia (1)
(1) Department of Preventive and Social Medicine, Faculty of Medicine, University of the Republic, (2) Oswaldo Cruz Foundation

Background/aims:
Cardiovascular disease (CVD) has been the leading cause of death globally for the past 20 years. Since Barker's work, substantial evidence has accumulated regarding the relationship between perinatal characteristics and the risk of developing CVD in later life. Both low birth weight and macrosomia are associated with an adverse metabolic profile in adulthood. Breastfeeding has been shown to have a protective role. The aim of this study was to establish cardiovascular risk patterns and perinatal variables as predictors of cardiovascular disorders in a cohort of adolescents from Uruguay, between 2004 and 2016.

Methods:
An exploratory study was conducted using classification and regression trees (CART) to classify perinatal variables in terms of predicting cardiovascular risk, in a sample of 272 adolescents enrolled in the "Estudio Longitudinal de Bienestar en Uruguay" (ELBU) cohort study. The sample was previously classified into two groups, high and low cardiovascular risk, based on alterations presented in non-invasive arterial measurements (systolic and diastolic blood pressure, heart rate, and peripheral vascular resistance). Perinatal variables from wave 1, anthropometric variables from waves 1, 3, and 4, and cardiovascular risk factors from wave 4 were used. ELBU was approved by the Faculty of Medicine´s Ethics Committee, University of the Republic, of Uruguay.

Results:
Obesity was classified as the main predictor of risk, constituting the root of the tree. Having obesity and having had macrosomia meant an 89% probability of belonging to the high-risk group. Low weight in infancy and the presence of breastfeeding for less than 6 months meant an 86% probability of belonging to the high-risk group, even if body fat percentage was normal.

Conclusions:
The exploratory analysis allowed us to establish potential cardiovascular risk patterns and estimate the factors that may lead to early cardiovascular damage.

Funding:

Key-words: (up to 5):
cardiovascular disease, cardiovascular risk, classification tree analysis

Abstract #00005605 en

High-sucrose diet and infection during pregnancy compromise gut function and fetoplacental development

Impact of Early Life Exposures and Environmental Pollutants

Champoudry da Silva O (1), Ferraz T (2), Cardoso LC (2), Paes AMA (1), Connor KL (2) (1) Federal University of Maranhão, São Luís (MA), Brazil, (2) Carleton U, Ottawa, Canada

Background/aims:
Latin American women face two significant risk factors during pregnancy: excessive sugar consumption and a high risk of viral infections. The maternal gut may be impacted by these exposures, with implications for nutrient absorption, immune defense, pregnancy outcomes, and fetoplacental growth. However, little is known about the combined impact of poor diet and infection on the maternal small intestine (SI) and pregnancy/offspring outcomes. We hypothesized that high-sucrose (HS) diet intake and viral infection during pregnancy would independently alter gut histomorphometry, resulting in suboptimal gut function and fetal development, while co-occurring exposures would lead to worse outcomes.

Methods:
Female C57BL/6J mice were exposed to HS diet (25% sucrose) or control (CON) diet eight weeks before and throughout pregnancy. Dams were injected with the viral mimic Poly(I:C) (POLY) or saline (VEH) 24h before sample collection at gestational day 18.5, resulting in four groups (n=3-5/group/GD). Maternal pregnancy body weight and food intake and fetoplacental weights, were recorded. Maternal SI sections were stained with H&E to quantify: villus height and width, crypt depth and width, and epithelial height. Effect of diet and infection on SI measures and fetal growth were quantified (Two-way ANOVA, Tukey's post hoc; $p<0.05$).

Results:
HS diet was associated with increased body weight during pregnancy compared to CON dams, but did not affect SI or fetal outcomes. In contrast, SI epithelial height was reduced in CONPOLY, in comparison to HSVEH, which could impair nutrient absorption. POLY infection also reduced fetoplacental weights. Co-exposure to HS diet and infection did not affect SI epithelial height, however crypt depth and width were increased, along with decreased fetoplacental weight compared to CONVEH.

Conclusions:
Maternal viral infection, both alone and in combination with HS diet, alters gut histomorphometry. These changes may compromise gut function, metabolism and nutrient absorption, potentially leading to insufficient resources for optimal fetoplacental growth and development.

Funding:
Natural Sciences and Engineering Research Council of Canada

Key-words: (up to 5):
maternal health, fetal development, infection, obesity

Abstract #00005610 en

Interaction of Diet-Induced Overweight and PAH Exposure: Effects on Testicular Homeostasis in a Rat Model

Impact of Early Life Exposures and Environmental Pollutants

FLORES QUIROGA JEREMIAS PABLO (1), LABIANO MARINA (1), DECHAMPS VICTORIA (1), HEINECKE FLORENCIA (1), GALARZA ROCIO (2), CORTEZ ANALIA (1), CASAL JUAN JOSE (3), MARTÍNEZ NORA ALICIA (4), WHITE VERONICA (1), FALETTI ALICIA (1)
(1) CEFYBO-UBA-CONICET, (2) CEREGeo-FCyT-UADER, (3) IFIBIO - UBA-CONICET / UCA, (4) IFIBIO - UBA-CONICET

Background/aims:
Previously, we observed that both overweight and exposure to 3-methylcholanthrene (3MC), an environmental polycyclic aromatic hydrocarbon(PAH), independently induced adverse effects on testicular architecture and sperm quality. We aimed to evaluate the impact of overweight and 3MC exposure on the structural and functional integrity of the testis in Sprague Dawley rats.

Methods:
Prepubertal male Sprague Dawley rats were fed either a standard diet(SD) or a cafeteria diet(CD) and were exposed to vehicle(V) or 3-methylcholanthrene(3MC, 0.1 mg/kg) three times per week for 40 days, resulting in four experimental groups: SDV, CDV, SD3MC, and CD3MC.
Spermatogenic cycle dynamics and testicular cell populations were evaluated histologically. The expression of steroidogenic enzymes was assessed by Western blot, and transcriptomic changes were analyzed using RNAsequencing. Genes with an adjusted p-value(padj)<0.05 and |log2foldchange|>1 were considered differentially expressed.

Results:
3MC altered the spermatogenic cycle by decreasing the early stages (I–VI) and accumulating stages VII–VIII($p<0.01$), while overweight affected the late maturation stages (XII–XIV)($p<0.05$) in non-exposed animals(CDV). Both overweight and 3MC decreased the number of spermatogonia and Sertoli cells, while only 3MC increased the number of Leydig cells in SD3MC($p<0.001$). Protein levels of steroidogenic enzymes STAR and CYP11A1 were decreased by 3MC ($p<0.05$), while 17β-HSD was increased in overweight rats exposed to 3MC ($p<0.05$). Overweight promoted the upregulation of Ndufa3 and Scd, linked to mitochondrial dysfunction and lipid metabolism alterations. 3MC exposure induced the expression of Cyp2a3 and Myod1 (xenobiotic response, impaired differentiation) and decreased Myb (a regulator of proliferation). Combined exposure enhanced inflammatory responses, with increased Ifit1bl and decreased Lilrb2 and Pirb expression, along with upregulation of genes involved in cell adhesion (Tlr2, Micb, Tmem176a/b).

Conclusions:
Our findings demonstrate that overweight and 3MC exposure synergistically impair testicular homeostasis, affecting spermatogenesis, steroidogenesis, and gene expression, highlighting the vulnerability of the male reproductive system to the convergence of metabolic disorders and environmental toxicants.

Funding:
BID-PICT-2020-Serie-A-nº-01125/PICT-2021-nº-I-A-00281-CONICET/PIP2022-23-n-CONICET.

Key-words: (up to 5):

Overweight / 3-Methylcholanthrene (3MC) / Testicular Homeostasis / Spermatogenesis / Steroidogenesis

Abstract #00005612 en

Role of basigin in early-preeclampsia related events

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Penailillo Reyna (1), Acuña Stephanie (1), Valdebenito Patricia (2), Choolani Mahesh (3), Kemp Matthew (3), Nardocci Gino (1), Monteiro Lara (1), Illanes Sebastian (1)
(1) Universidad de los Andes, (2) IMPACT, Center of Interventional Medicine for Precision and Advanced Cellular Therapy, (3) National University of Singapore

Background/aims:
Basigin (BSG) is a highly glycosylated type I transmembrane protein involved in the induction of matrix metalloproteinase (MMP) synthesis, extracellular matrix degradation, tissue remodeling, and angiogenesis. Preeclampsia (PE) is characterized by deficient trophoblast invasion of the decidua and incomplete remodeling of the spiral arteries. To investigate whether BSG plays a role in PE-related processes in early placentation, it is essential to study its expression in first-trimester trophoblast cells and mesenchymal stem cells isolated from menstrual fluid (MenSCs), as well as its impact on cell migration, angiogenesis, and invasive capacity.

Methods:
MenSCs were isolated from menstrual fluid of women with (Control group, n=4) and without PE history (PE group, n=3). BSG and MMP2 expression were determined in MenSCs and HTR-8/SVneo during hypoxic conditions after 24 and 48h of culture by qPCR and western blot. Small interfering (si) RNA transfection downregulates BSG in HTR-8/SVneo. Transmigration and angiogenic capacity were assessed in HTR-8-BSG-depleted cells using transwell and Matrigel-based tube formation assays. A 3D invasion assay was performed to determine invasion capacity of HTR-8-BSG depleted cells induced by MenSCs. This study was approved by Ethical Scientific Committee of Universidad de los Andes CEC2023039.

Results:
BSG protein expression was increased in HTR-8 cells under hypoxic conditions (1%O2, p=0.01 Kruskal-Wallis test; n=4) compared to 21%O2. MenSCs did not show differences between Control and PE group. HTR-8/SVneo-BSG-depleted cells showed a reduced transmigration capacity (0.63±0.12 vs 1±0.0, p=0.03 Mann-Whitney test; n=4), but no changes in MMP2 protein level were observed. Angiogenesis and invasion capacity did not show significant changes (p>0.05, Mann-Whitney test; n=3-2).

Conclusions:
Our results suggest that BSG expression is upregulated in trophoblast cells under hypoxic conditions. Moreover, BSG contributes to trophoblast migration but may not directly influence other processes such as invasion or angiogenesis, highlighting a potential, but specific, role of BSG in mechanisms associated with preeclampsia development

Funding:
FONDECYT Postdoctoral #3230201, FONDECYT Regular #1241103, FONDECYT Regular #1230932

Key-words: (up to 5):
Basigin, trophoblast, mesenchymal stem cells

Abstract #00005615 en

The significance of the placenta for Mapuche culture in the context of intercultural protocols implemented in the Chilean Health System.

Public Health Policies Across the Life Cycle.

Cheuquelao-Fica Javiera (1), Painequeo-Painequeo Neftalí (2), González-Ortiz Marcelo (3)
(1) Programa de Magíster en Salud Sexual y Reproductiva, Universidad de Concepción, Chile., (2) Museo Mapuche Juan Cayupi Hechicura, Cañete, Chile, (3) Laboratorio de Investigación Materno-Fetal (LIMaF), Universidad de Concepción, Chile.

Background/aims:
Among the ancestral practices of the Mapuche people in relation to pregnancy and birth, the burial of the placenta is a significant moment. For this reason, technical note 189 has been implemented in the Chilean health system, which consists of a protocol for the delivery of the placenta to Mapuche women. A problem in implementing intercultural protocols is the unilateral definition of health policies, without equitably considering the knowledge of the communities.

objective: To collect experiences about practices associated with the placenta in the Mapuche women and to determine the main barriers to intercultural practices in the health system.

Methods:
Qualitative study, using in-depth interviews for Mapuche women and intercultural facilitators. The Mapuche women interviewed were from the Biobío and La Araucanía regions (Chile). The study was approved by the Ethics and Scientific Committee from Concepción Health Service (CEC-SSC 22-03-05), and women signed informed consent.

Results:
Not all Mapuche women are informed about the technical note 189 or about the requirements for requesting their placenta. The presence of an intercultural facilitator in the hospitals is relevant because it guarantees better treatment and respect for Mapuche culture from the health team. It is also noted that burying the placenta requires the well-being of the family and community and the availability of ancestral territory. Therefore, Mapuche women living in urban territories have greater difficulty practicing cultural traditions related to birth and placenta.

Conclusions:
For the health system, the placenta is an organ considered biological waste, while for Mapuche culture, it is a relevant organ, beyond pregnancy and birth, that connects the newborn to the earth, their family, and their community. However, Mapuche women do not receive all the information about the placenta protocol early. Furthermore, health teams need more education and training about Mapuche culture related to gestation, birth, and placenta.

Funding:
UCO 2295 Interculturality project, Universidad de Concepción, Chile.

Key-words: (up to 5):
intercultural health, placenta, birth, Mapuche.

Abstract #00005623 en

The long-lasting effect of gestational hypoxia on brain content of water in the prefrontal cortex in the guinea pig model of fetal growth restriction.

Impact of Early Life Exposures and Environmental Pollutants

Meza-Vilches Osvaldo (1), Muñoz-Guzmán Fernanda B. (2), Palma C. Daniel (2), Borgoño S. Julian (3), Orellana Luis Octavio (2), Herrera Emilio A. (4), González-Candia Alejandro (3)
(1) Laboratorio de Neuroprogramación Fetal, Instituto de Ciencias de la Salud, Universidad de O'Higgins., (2) Laboratory of Fetal Neuroprogramming, Institute of Health Sciences, University of O'Higgins., (3) Laboratory of Fetal Neuroprogram, Institute of Health Sciences, University of O'Higgins, (4) Vascular Function & Reactivity Lab, Pathophysiology Program, ICBM, Universidad de Chile

Background/aims:
The blood-brain barrier (BBB) is formed by endothelial cells. Variations in the protein transport components of the cells that form the BBB, lead to an increased passage of the ions and water into the brain. Our hypothesis is that gestational hypoxia modifies the permeability of the BBB through changes in the electrolytic protein transport present in the brain's endothelium in newborn and juvenile gestated under hypoxia.

Methods:
This study was approved by the Institutional Bioethics Committee (certificate 20418-MED-UCH) and included four experimental groups, divided into two stage, normoxic (Nx1, n=5) and hypoxic neonates (Hx1, n=5) and normoxic (Nx75, n=5) and hypoxic juveniles (Hx75, n=5). All groups were introduced into a hypobaric chamber under conditions of normoxia (N, controls, 720 torrs , ~580 m) or hypoxia (H, 470 torrs, ~3800 m) during gestation until birth. Brain samples were collected at birth on day 1 (Nx1, Hx1) and juveniles on day 75 (Nx75, Hx75) of life. The protein levels of MMP-2, MMP-9, NHE-1, NHE-3, and NKCC were evaluated by western blot and immunohistochemistry (IHQ) in the prefrontal cortex. The water content in the brain was measured by the dehydration of the prefrontal cortex tissue, and a non-parametric student t-test was used. Significative differences were considered when $p<0.05$.

Results:
Increased protein levels of NHE-1, NKCC, and higher water content were observed in Hx1 compared to Nx1 in the prefrontal cortex. No significant changes in MMP-2 and MMP-9 expression were found between groups. Additionally, all protein levels of NHE-1, NHE-3, and NKCC were normalized in the juvenile stage.

Conclusions:
NHE-1, NKCC protein levels and water content were increased in hypoxic newborn in the prefrontal cortex. No changes were observed in protein expression in MMP2 and MMP9 between groups analyzed, and all levels of NHE-1, NHE-3, and NKCC were normalized in the juvenile stage, respectively.

Funding:
Fondecyt Regular 1241626 **Key-words: (up to**

5):

Perinatal hypoxia, edema, BBB permeability, neurovascular unit, DoHAD hypothesis

Abstract #00005632 en

Longitudinal Association Between Human Milk Macronutrient Intake and Infant Growth During the first 8.5 Months: A Multicenter Cohort Study

Role of Infant and Young Child Feeding Practices on Long-Term Health

Figueiredo Amanda Caroline Cunha (1), Campos Adriana Divina de Souza (2), Silva Gabriela Torres (2), Schneider Bruna (2), Polessa Daniela Paula (2), Mucci Daniela (2), Moore Sophie E. (3), Islam Munirul (4), Michaelsen Kim (5), Mølgaard Christian (5), Allen Lindsay H. (6), Hampel Daniela (6), Kac Gilberto (2)

(1) Federal University of Rio de Janeiro/Serra dos Órgãos University, (2) Federal University of Rio de Janeiro, (3) King's College London/MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine, (4) International Centre for Diarrhoeal Disease Research, (5) University of Copenhagen, (6) University of California Davis

Background/aims:

Recent studies show that human milk (HM) macronutrients play an important role in infant growth. However, studies adjusting HM macronutrients for HM intake are scarce. Thus, this study aimed to evaluate the longitudinal association between HM macronutrient intake and infant growth.

Methods:

This study includes 531 mother-infant dyads from the Mothers, Infants and Lactation Quality (MILQ) study from Bangladesh (n=158), Brazil (n=117), Denmark (n=178), and The Gambia (n=78). The participants were followed at visit 1–3.5 months (M1), 3.5–6 months (M2), and 6–8.5 months (M3), resulting in a total of 1,407 observations. HM macronutrients were measured by near-infrared spectroscopy at visit M1. HM intake was assessed at visit M1 by the stable isotope dilution 'dose-to-mother' method, except in Denmark, where test weighing was used. HM macronutrient intake (g/day) was estimated as the product of each macronutrient concentration (g/L) and HM volume (g/day), considering the HM density of 1.03 g/mL. Infant growth was evaluated using the WHO Growth standards weight-for-age (WAZ), length-for-age (LAZ), and weight-for-length (WLZ) z score at visits M1, M2, and M3. Statistical analyses included linear mixed-effects models adjusted for site and mother-infant confounders. All sites received ethical approval, and informed consent was obtained (Bangladesh=PR-17085; Brazil=2.086.708; Denmark=H-17015174; Gambia=22768).

Results:

The median (IQR) of macronutrient intake (g/day) at the M1 visit was 7.2 (5.9-8.7) for protein, 53.3 (46.8-61.4) for carbohydrates, and 25.1 (18.5-33.9) for lipids. Positive Longitudinal associations were observed between HM protein intake and WAZ (β=0.083, P<0.001), LAZ (β=0.044, P=0.004), and WLZ (β=0.082, P<0.001). HM carbohydrate intake was associated with higher WAZ (β=0.034, P<0.001), LAZ (β=0.016, P<0.001,) and WLZ (β=0.036, P<0.001). A positive association was also observed between HM lipid intake and WAZ (β=0.014, P<0.001) and WLZ (β=0.018, P<0.001).

Conclusions:

These results revealed that HM macronutrient intake may be associated with infant growth based on data from a multicenter cohort.

Funding:

Bill & Melinda Gates Foundation and Carlos Chagas Filho Foundation for Research Support of Rio de Janeiro State (FAPERJ).

Key-words: (up to 5):
(1) Human milk; (2) Infant Growth; (3) Cohort; (4) Milk volume (5) Macronutrient intake.

Abstract #00005635 en

Undernutrition during adolescence impers liver function as long term-consequence in male and female rats without changing redox balance

Role of Infant and Young Child Feeding Practices on Long-Term Health

de Oliveira Júlio Cezar (1), Saint Paul Joskame (1), Santos Thiara Chaves (1), Souza Mariele de Oliveira (1), Ribeiro Antonio José Rocha (1), Kipper Ana Caroline Schoenberger (1), Dias Ginislene (1), Bello Alexandre Aymberé (2), Silva Geovana Fazolo (1), Maia Sara Vieira (2), Sinhorin Valéria Dornelles Gindri (2)
(1) Instituto de Ciências da Saúde, Universidade Federal de Mato Grosso (UFMT), Sinop, (2) Laboratório Integrado de Pesquisas Químicas, Universidade Federal de Mato Grosso (UFMT), Sinop

Background/aims:
Malnutrition is yet a drastic problem, affecting around 10% of the world population, which makes it a serious social and public health problem. In critical stages of life development malnutrition can program long-term metabolic dysfunction compromising individuals throughout adulthood. Herein, we aimed to assess the long-term effects of undernutrition during adolescence on the liver's function and glucose homeostasis in male and female rats.

Methods:
Male and female Wistar rats underwent undernutrition by 30 days (food reduction by 50% (FR50 group) from ad libitum amount offered to control (CONT) rats since 30- until 60-days old. At adulthood the glucose and insulin tolerance tests were performed, and at 120-days old, rats were euthanized to assess liver redox balance (catalase, CAT; superoxide dismutase, SOD and glutathione S-transferase, GST) and function (aspartate aminotransferase, AST and alanine transaminase, ALT). Data were performed following the recommendation approved by ethics committee (protocol #23108.021234/2024-73) and submitted to Shapiro-Wilk test to assess Gaussian distribution and to the two-way ANOVA, followed by Tukey's post-test, with $P<0,05$ as significant.

Results:
At 60-days old, FR50 rats were smaller than their counterparts (male: –36.4% and female: –22.7%; $P<0.001$); while at 120-days old, there was no difference between CONT versus FR50 rats ($P>0.05$). In relation to their counterparts, the FR50 male and female rats display high glucose tolerance (~23%, $P<0.05$) and high insulin sensitivity (~3-fold, $P<0.01$), as well increased levels of ALT and AST (~23%, $P<0.05$) and reduction in CAT (38%, $P<0.01$) in male and increased SOD in female (36%, $P<0.05$).

Conclusions:
Undernutrition during adolescence program rats in both sexes to have high insulin sensitivity and liver dysfunction as long-term consequence, which can drive rat's metabolism to be more proneness to obesity onset if exposed unbalanced diet.

Funding:
This work did not have funding.

Key-words: (up to 5):
Metabolic programming, hepatic dysfunction, glucose homeostasis.

Abstract #00005636 en

Preterm birth, intrauterine growth restriction, and respiratory health of 9-year-old Malawian children

Big Data and Cohorts in DOHaD Research.

Virtanen Eeva (1), Näsänen-Gilmore Pieta (2), Ashorn Per (3), Ashorn Ulla (3), Mangani Charles (4), Kajantie Eero (1) (1) University of Oulu, (2) Finnish Institute for Health and Welfare, (3) University of Tampere, (4) Kamuzu University of Health Sciences

Background/aims:
Preterm birth (<37 gestational weeks) or being born small for gestational age (SGA, birth weight < 10th percentile) may have a negative effect on lung development. Regardless of over 80% of preterm and SGA births taking place in low- and middle-income countries, the association has been mainly established by studies coming from high-income countries. Therefore, we assessed lung function and respiratory symptoms among 9-year-old Malawian children born preterm or small for gestational age (SGA).

Methods:
In a follow-up of the international Lipid-based Supplementation trial (iLINS-DYAD-M), we assessed lung function and respiratory symptoms of 9-year-olds born preterm (n=41) and term SGA (n=152), with children born term AGA (n=486) as reference. Primary outcomes were forced expiratory volume in 1 second (FEV1) and the ratio of FEV1 to forced vital capacity (FEV1/FVC), expressed in Global Lung Function Initiative z-scores and wheeze by ISAAC questionnaire. We used multiple linear or logistic regression with adjusting for socioeconomic and pregnancy-related factors.

Results:
Compared with term AGA children, mean difference (95% CI) in zFEV1 was 0.15 (-0.07, 0.38) for T-SGA and -0.16 (-0.55, 0.22) for PT. Corresponding differences for zFEV1/FVC were 0.21 (-0.03, 0.55) and -0.30 (-0.64, 0.05). In term AGA, term SGA and PT groups, numbers of children with FEV1 below -1.64SD were 179 (36.8%), 47 (30.9%), and 17 (36.2%). The odds ratio for wheeze was 2.97 (1.41, 6.25) for T-SGA and
3.62 (1.13, 11.63) for PT group.

Conclusions:
We found no association between preterm birth or SGA and airflow among 9-year-old Malawian children. However, in these groups the risk for wheeze appears to be higher than in controls. High percentage of Malawian children have FEV1 values below normal levels, indicating possible public health concern that needs to be further researched.

Funding:
Research Council of Finland, Signe and Ane Gyllenberg, Sigrid Jusélius and Ahokas Foundations, Finska Läkaresällskapet, Foundation for Pediatric Research

Key-words: (up to 5):
preterm birth, small for gestational age, low- and middle-income countries, lung health

Abstract #00005639 en

Determinants of Bone Health in Women in Rural South India

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Joseph Shama V (1), Prabhu Manohar Prasad (1), Nagabharana TK (2), Kumar GS (1), Yashodha G (1), Susheela N (1), Ningaraja HN (1), Kiran KN (1), Bhat G (1), Matthews Stephen G (3), Krishnaveni GV (4), Kumaran Kalyanaraman (5)
(1) Swami Vivekananda Youth Movement , (2) Institute of Public Health, (3) University of Toronto, (4) CSI Holdsworth Memorial Hospital, (5) University of Southampton

Background/aims:

Background/aims: Bone mineral density (BMD) is dependent mainly on calcium- and Vit D-rich foods intake, sun exposure and physical activity. Nutritional status and socioeconomic status (SES) may also impact BMD. Research has shown that maternal bone health influences offspring bone health, possibly through nutrient availability and epigenetic mechanisms. We examined possible determinants of BMD in rural women of childbearing age in India as part of the Healthy Life Trajectories Initiative (HeLTI), which aims to investigate whether a longitudinal intervention starting preconceptionally influences offspring body composition.

Methods:

Methods: Total BMD was measured using Dual energy Xray absorptiometry (DEXA). Consumption of calcium and Vit D containing foods (dairy products, non-vegetarian foods and eggs) and SES were determined using standardized questionnaires. Nutritional status was determined by anthropometry and hemoglobin (Hb) measurement. Written consent was obtained from participants (Ethics committees-CSIHMH/ERU2018/1, IRB11/2017-18). Linear regression and t-tests were used to examine relationships between various exposures and BMD.

Results:

Results: DEXA scans were conducted in 165 women. Average BMD was 1.023±0.08 g/cm2. Average BMI and Hb levels were 22.5±4.8 and 11.9±1.5 g/dL respectively. The majority of women had BMD values within the normal range, while ~31% had a T-score of between -1 and -2.4 indicating osteopenia, and ~2% had a T score of ≤-2.5 indicating osteoporosis. There was a significant direct association between BMI and BMD ($P < 0.001$). However, there were no relationships between dietary factors, Hb, or SES and BMD.

Conclusions:

Conclusions: Similar to other studies from India and elsewhere, there was a direct relationship between concurrent BMI and BMD. BMD in women in rural South India was not associated with dietary factors, Hb or SES. Further research to understand determinants of BMD in this population will involve examining relationships with Vit D concentrations, and considering sunlight exposure.

Funding:

Funding: DBT, India (BT/MED/WHO-CIHR/2014); CIHR (NDN-151554) **Key-words: (up to 5):**

BMD, Nutrition, India, Women, Rural

Abstract #00005643 en

Maternal Oral Dysbiosis Disrupts Offspring Gut Colonization and Alters Early-Life Behavior

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Watanabe Natsuru (1), Mikami Katsunaka (1), Yamamoto Kenji (1), Kamada Nobuhiko (2) (1) Tokai University, (2) The University of Michigan Medical School

Background/aims:
Early-life gut microbiota composition is critical for neurodevelopmental health. Recent evidence suggests that maternal microbiota, including non-gut commensals such as oral bacteria, significantly contribute to the initial colonization of the infant gut microbiota. Dysbiosis of maternal oral microbiota may therefore impact offspring gut colonization and influence neurodevelopment and behavior. This study aimed to investigate whether maternal oral dysbiosis affects early-life gut microbiota composition and alters behavioral traits in offspring.

Methods:
We induced experimental periodontitis and oral dysbiosis in female mice by ligature placement before mating. Offspring born to these dams and control dams were evaluated. To assess early behavioral traits, anxiety-like behavior was examined at 4 weeks of age using the marble burying test. As a positive control for severe microbiota disruption, offspring from dams treated with the antibiotic cefoperazone were also analyzed.

Results:
Offspring from both antibiotic-treated and periodontitis dams showed a significant reduction in marble burying behavior compared to controls, suggesting an early-life behavioral alteration. No differences in short-term memory or general activity levels were observed, indicating that reduced marble burying was not due to motor deficits.

Conclusions:
Maternal oral dysbiosis alters offspring gut microbiota composition and affects early-life anxiety-like behavior. Early disruption of gut microbiota, even if limited to specific microbial populations, may have lasting effects on neurodevelopment. These findings highlight the importance of maternal microbiota health, particularly oral microbiota, in shaping offspring brain and behavioral outcomes, offering a potential target for early preventive interventions.

Funding:

Key-words: (up to 5):
gut microbiome, microbiota-gut-brain axis, maternal transmission, oral dysbiosis, behavior

Abstract #00005644 en

Neonatal body composition and its correlations with maternal nutritional status in rural South India

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Prabhu Manohar Prasad (1), Ghattu Krishnaveni (2), Suryanarayana Kumar Gavali (1), Nagabharana TK (3), Joseph Shama (1), G Yashodha (1), HN Ningaraja (1), Golsangi Sangita (1), KN Kiran (1), Bhat Gurudath (1), Shah Prakesh (4), Fall Caroline (5), Matthews Stephen (4), Kumaran Kalyanaraman (5)
(1) Swami Vivekananda Youth Movement, (2) Epidemiology Research Unit, CSI Holdsworth Memorial Hospital, (3) Institute of Public Health, Bengaluru, (4) University of Toronto, (5) University of Southampton

Background/aims:
Research in India has shown that poor maternal nutritional is associated with impaired foetal development, leading to an increased vulnerability to cardiometabolic disease in later life. Some of this increased risk appears to come from changes in newborn body composition; the typical Indian new born tends to be light and thin with a low lean body mass, but relatively adipose (the 'thin-fat' Indian). The Healthy Life Trajectories Initiative (HeLTI) is a multi-country trial that aims to investigate whether a multi-faceted longitudinal intervention starting preconceptionally reduces childhood adiposity. The Indian project is based in 105 villages near Mysuru in South India. We report preliminary findings of neonatal body composition and their associations with maternal nutritional status.

Methods:
We measured neonatal body composition (n=287) using Dual Energy X-ray Absorptiometry (DEXA) and examined its relationship with their mothers' body mass index (BMI) and haemoglobin levels during preconception and early pregnancy. Informed consent was obtained from participants (Ethics #CSIHMH/ERU2018/1, IRB11/2017-18).

Results:
The mean (SD) weight was 2.84 kg (0.53), lean mass was 2.41 kg (0.41) and fat mass was 0.51 kg (0.16). Mean (SD) total fat percent was 17.1% (2.8). Maternal preconception BMI was directly correlated with neonatal lean mass, fat mass and fat percent ($P<0.05$ for all). Maternal preconception haemoglobin was directly correlated with lean and fat mass ($P<0.05$ for both) but not with fat percent. The results were similar for maternal BMI and haemoglobin during pregnancy. Gestational age was correlated with neonatal fat mass ($P=0.03$) but not with lean mass.

Conclusions:
Maternal nutritional status both before and during pregnancy is associated with neonatal body composition in rural Indians. It will be interesting to evaluate the effect of the HeLTI preconceptional interventions on neonatal body composition.

Funding:
DBT India (BT/MED/WHO-CIHR/2014); CIHR Canada (NDN-151554)

Key-words: (up to 5):
Neonatal, Body composition, Pre-conceptional interventions, HeLTI, India

Abstract #00005646 en

Challenges And Facilitators To Offer Social Support During Pregnancy: A Qualitative Study In Rural Southern India

Public Health Policies Across the Life Cycle.

Nagabharana TK (1), Joseph Shama V (2), Prabhu Manohar Prasad (2), MC Ramya (1), Kehoe Sarah H (3), Vogel Christina (4), Barker Mary (3), HD Fall Caroline (3), Gavali Suryanarayana Kumar (2), G Matthews Stephen (5), Kumaran Kalyanaraman (3), Krishnaveni GV (6)
(1) Institute of Public Health, (2) Vivekananda Memorial Hospital, (3) University of Southampton, (4) City University of London, (5) University of Toronto, (6) CSI Holdsworth Memorial Hospital

Background/aims:
Maternal health is crucial for fetal development. Poor fetal growth increases risk of cardiometabolic disorders in later life. Social support during pregnancy has shown to improve pregnancy outcomes. The Healthy Life Trajectories Initiative (HeLTI) employs multifaceted interventions from preconception through postpartum to optimise fetal growth. Previous qualitative research explored sources of social support during pregnancy in rural South India. Family/ community offered support in six domains: General, Nutrition, Medical, Guidance, Tangible and Emotional. This study explores barriers and facilitators to offer social support.

Methods:
A total of 13 Focus Group Discussions (FGDs) involving 83 participants were conducted with women of reproductive age, married men, community leaders, mothers and mothers-in-law, and community health workers (CHWs). Data were analyzed thematically to identify broad themes and subthemes. Institutional Ethics Committee of CSI Holdsworth Memorial Hospital, Mysuru; and Vivekananda Memorial Hospital, Saragur approved study.

Results:
The main barriers were: 1. lack of awareness of the need for self-care, including general health, diet and hygiene; and 2. financial challenges, with women working until late stages of pregnancy. Intervention/facilitator to address these barriers was mainly improved health awareness through 1. accessible health camps focusing on health literacy; and 2. improved CHWs health outreach. It is interesting to note that while efforts to improve health literacy was generally wished for, CHWs' expressed, their advice on diet, hygiene and healthcare access faced reluctance from the women and families, especially among the tribal community.

Conclusions:
Government services addressing resource gaps, couple with targeted health literacy efforts by health workers will enhance social support during pregnancy. Focused training of CHWs on providing advice on general health and mental health certainly support this effort. Study highlights the underlying challenge to bring about the change in attitude and lifestyle in addition to poor health literacy.

Funding:
DBT, India_(BT/MED/WHO-CIHR/2014); CIHR _(NDN-151554).

Key-words: (up to 5):

Family support, Pregnancy care, Pregnancy support, Social support, Sources of support

Abstract #00005650 en

Adipokines and Newborn Body Composition in Gestational Diabetes Mellitus (GDM) Pregnancies: PEAPOD Study

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Periyathambi Nishanthi (1), Bagias Christos (1), Asres Haile (2), Sukumar Nithya (1), Weldeselassie Yonas (2), Saravanan Ponnusamy (1)
(1) University of Warwick, (2) The Open University

Background/aims:
Gestational diabetes mellitus (GDM) exposure is associated with altered foetal growth. The biological mediators of new-born's fat mass (FM) and fat-free mass (FFM) remain unclear. We investigated whether mid-pregnancy maternal adipokine (leptin and adiponectin) levels have any influence on neonatal FM and FFM with and without GDM.

Methods:
We analysed data from the prospective PEAPOD cohort (966 mother-infant pairs; 120 GDM-exposed). New-born body composition was assessed within 72 hours using air-displacement plethysmography (n=554). FM index (FMI) and FFM index (FFMI) were calculated (kg/m²) to account for length. GDM was diagnosed using NICE criteria. In a sub-group (n=178), both cord blood and PEAPOD measurements were available. Maternal fasting adipokines (24-28 weeks) and cord blood adipokines were measured in this sub-group. Associations between maternal adipokines and neonatal body composition were examined in regression models, stratified by GDM status. Models were adjusted for maternal age, ethnicity, BMI, parity, gestational age at delivery, sex, and birthweight. Benjamini-Hochberg test was used for multiple testing correction.

Results:
New-borns born to GDM mothers had lower birthweight (-164.1g, 95%CI: -268.2, -59.9; p=0.002), lower FFM (-147.5g, 95% CI: -234.5, -60.4; p<0.001) but similar FM (31.7g, 95% CI: -70.4, 7.03; p=0.11) and FMI (-0.09kg/m2, p=0.12) compared non-GDM. The FFMI was also marginally lower (-0.24kg/m2, p=0.08). In the sub-group, while the new-born FMI and FFMI were similar between GDM and non-GDM, higher maternal leptin in GDM mothers was strongly associated with reduced FFMI compared to non-GDM in an interaction analysis (β= -0.93; p=0.01). No significant difference in maternal and cord biomarkers observed between GDM and non-GDM.

Conclusions:
Our findings suggest that elevated maternal leptin levels in GDM may be a mediator of reduced neonatal FFMI. Whether this reduced FFM/FFMI persists beyond birth or explains the future metabolic risk in the offspring requires further studies.

Funding:
National Institute for Health Research (NIHR); Sir Jules Thorns

Key-words: (up to 5):
GDM, Maternal adipokines, neonatal body composition

Abstract #00005651 en

Maternal Hypothyroxinemia and Increased Tendency to Obesity in Offspring: Examining Behavioral Changes

Impact of Early Life Exposures and Environmental Pollutants

Millaleo Bárbara (1), Regaldiz Alejandro (2), Gallegos Andres (3), Riedel Claudia (2), Opazo M. Cecilia (3) (1) Universidad de las Américas., (2) Universidad Andres bello, (3) Universidad de las Americas

Background/aims:
Maternal health during gestation is essential for fetal development. Changes in the intrauterine environment can increase offspring susceptibility to chronic diseases, such as obesity, later in life. Maternal nutrition and endocrine health are critical in programming eating behaviors and predisposition to diet-induced obesity. Maternal hypothyroxinemia (HTX), marked by low thyroxine levels, has detrimental effects on offspring, increasing their susceptibility to obesity. While food intake regulation is key for preventing obesity, the impact of HTX on eating behavior remains unclear. This study aimed to assess the behavioral changes linked to obesity susceptibility in offspring gestated under HTX or normal conditions.

Methods:
Male and female C57BL/6 mice, gestated in HTX or normal conditions, underwent a 16-week dietary intervention. One subgroup was fed a personalized Western-like diet (CAF-P); the other received a standard diet. Body weight and food intake were recorded throughout. Behavioral changes were assessed through a social vs. food preference test, physical activity and strength tests, and a marble burying test.

Results:
Offspring exposed to HTX conditions and subsequently fed the CAF-P diet demonstrated significantly greater weight gain compared to control offspring. Also exhibited a pronounced preference for food-related stimuli over social stimuli, indicating a shift in motivational salience towards palatable foods. Furthermore, the HTX group displayed an increased preference for sweet snacks when maintained on the CAF-P diet. Importantly, no significant differences were observed between groups in measures of physical activity or muscle strength, suggesting that the observed weight gain and altered food preferences were not attributable to changes in activity levels or physical capacity.

Conclusions:
Maternal hypothyroxinemia increases susceptibility to diet-induced obesity in offspring, possibly through alterations in food preferences and eating behavior.

Funding:
UDLA (UDLA DI-08/22 Y PIR202425), Centro de Investigación en Ciencias Biológicas y Químicas (UDLA), Programa de Magíster en Ciencias Biológicas y Químicas, Universidad de las Américas.

Key-words: (up to 5):
maternal hypothyroxinemia, cafetería diet, obesity, behavioral tests.

Abstract #00005653 en

Prenatal Stress Drives Neuroinflammation in the Postpartum Prefrontal Cortex of Dams and Their Offspring

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Luft Carolina (1), Potter Spagnol Herika Raquel (1), Vivan Tonial Giovana (1), Bonatto Arlaque Thiago (1), Alvim Stocchero Bruna (1), Kaiber Daniela (1), Rodrigues de Oliveira Jarbas (1), Wendt Viola Thiago (1), Fagundes Donadio Marcio Vinicius (2)
(1) PUCRS, (2) UIC

Background/aims:
The postpartum period is a critical window for neurodevelopment in both dams and their offspring, where prenatal stress (PNS) can profoundly impact the central nervous system (CNS). PNS triggers neuroinflammatory responses by activating pathways, such as the inflammasome, that upregulate pro-inflammatory cytokines. These cytokines disrupt neural homeostasis in the prefrontal cortex (PFC), a region vital for behavioral regulation, increasing the risk of neuropsychiatric disorders. In dams, postpartum neuroinflammation may impair maternal care and CNS function, while in offspring, it can alter developmental trajectories, with potential sex-specific effects. This study aimed to assess the postpartum effects of gestational stress on neuroinflammatory gene expression, including inflammasome-related markers, in the PFC of non-pregnant females, dams, and male and female offspring at postnatal day 10 (PND10).

Methods:
Female BALB/c mice were divided into four groups (Ethics Committee #11638): non-pregnant control (CON-NP), restraint-stressed non-pregnant (S-NP), pregnant control (CON-PNS), and prenatal restraint stress (PNS). On PND10, PFC tissue was collected from non-pregnant females, dams, and male and female offspring. Gene expression of neuroinflammatory markers and inflammasome components was evaluated.

Results:
Gestational stress and pregnancy modulate postpartum neuroinflammation in the PFC, with increased IL-10 in dams and inflammasome activation in PNS dams and female offspring. Sex-specific IL-6 reductions in offspring suggest differential neuroinflammatory responses. Specifically, pregnancy (CON-PNS, PNS) increased IL-10 expression in dams' PFC compared to non-pregnant females ($p<0.05$). PNS dams showed elevated caspase-1 and ASC expression compared to S-NP and CON-PNS ($p<0.05$). In PND10 offspring, PNS males had decreased IL-6 expression compared to CON-PNS males ($p<0.05$), and CON-PNS females had lower IL-6 than CON-PNS males ($p<0.05$). PNS females showed increased caspase-1 expression compared to CON-PNS females ($p<0.05$).

Conclusions:
Postpartum neuroinflammation, driven by pregnancy and gestational stress, alters PFC gene expression with distinct maternal and offspring profiles. Inflammasome activation and sex-specific cytokine responses observed may elevate neuropsychiatric risks across generations.

Funding:
CAPES– Finance Code 001, and FAPERGS.

Key-words: (up to 5):
Cytokines, Inflammasome, Sex Differences

Abstract #00005654 en

p-AKT–UCP1 axis activation in interscapular brown adipose tissue mitigates metabolic dysfunction induced by high-sucrose diet in small litter size rats

Role of Infant and Young Child Feeding Practices on Long-Term Health

Jesus de Deus Isabela (1), Martins de Andrade Fagundes Miliane (2), Letícia Silva Juliana (1), Rezende Ribeiro de Abreu Aline (1), Silveira Breguez Gustavo (2), Antunes Silva Ângela (3), Cristina da Silva Oliveira Siqueira Érika (3), Martins Carneiro Cláudia (4), Caldeira Costa Daniela (5), Paula-Gomes Sílvia (6), Barbosa de Queiroz Karina (2)
(1) Postgraduate Program in Health and Nutrition, Federal University of Ouro Preto, (2) Department of Food, Federal University of Ouro Preto, (3) Animal Science Center, Federal University of Ouro Preto, (4) Research Center in Biological Sciences/NUPEB, Federal University of Ouro Preto, (5) Department of Biological Science, Federal University of Ouro Preto , (6) Department of Biological Science, Federal University of Ouro Preto

Background/aims:
Early-life nutritional environments can induce metabolic imprinting, influencing susceptibility to chronic diseases. This study aimed to explore whether early-life metabolic imprinting via small litter size can modulate thermogenic responses in interscapular brown adipose tissue (iBAT) and mitigate the development of insulin resistance (IR) in young rats challenged with a high-sucrose diet (HSD).

Methods:
After approval by the Ethics Committee on Animal Use of the Federal University of Ouro Preto (UFOP), Protocol 2245040518, Wistar rats (n=48) were assigned to control (eight pups/dam; CL) and small litter (four pups/dam; SL) groups. Post-weaning (21 days), they were divided into four dietary groups: (i) standard diet (STD, chow diet) from CL, or (ii) SL; (iii) HSD (30% sucrose) from CL, or (iv) SL, for eight weeks. After the treatment period, iBAT and serum were collected for biochemical, molecular, and histological analyses.

Results:
HSD exposure in CL animals led to iBAT hypertrophy ($P < 0.001$), IR ($P < 0.001$), and oxidative stress ($P < 0.01$). In contrast, SL animals fed HSD showed improved insulin signaling characterized by increased p-AKT (Ser473) ($P < 0.001$), elevated UCP1 expression ($P < 0.001$), and signs of iBAT hyperplasia($P < 0.001$), even with reduced PGC1-α content ($P < 0.01$). HSD-SL animals also exhibited decreased PKA substrate phosphorylation ($P < 0.001$) and lower circulating free fatty acids ($P < 0.05$), coinciding with diminished lipid peroxidation in iBAT ($P < 0.001$). These results suggest that small litter size induces long-lasting adaptations enhancing iBAT thermogenic capacity and protecting against HSD-induced metabolic derangements.

Conclusions:
Metabolic imprinting through early-life overnutrition conferred by small litter size promotes iBAT activation and improves systemic insulin sensitivity in rats challenged with a HSD, likely through mechanisms involving p-AKT signaling and modulation of PKA activity.

Funding:
This study was financed by CAPES code 001, FAPEMIG APQ-04983-22, CCA-UFOP, and UFOP.

Key-words: (up to 5): metabolic imprinting; interscapular brown adipose tissue; high-sucrose diet; insulin signaling; oxidative stress.

Abstract #00005660 en

Pre-conceptional exposure to low doses of malathion later impairs placentation and leads to placental oxidative stress in female Wistar rats

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Fernandes Glaura (1), Frigoli Giovanna (2), Costa Ivana (2), Greghi Julia Rodrigues (3), Tenorio Pedro (4), Martins Maria (3), Andrade Fábio (4), Favaron Phelipe Oliveira (5)
(1) Department of General Biology - State University of Londrina - UEL, (2) Department of Immunology, Parasitology and General Pathology - State University of Londrina Brazil, (3) Department of Veterinary Clinicas - State University of Londrina - Brazil, (4) Department of Histology - State University of Londrina - Brazil, (5) Department of General Biology - State University of Londrina - Brazil

Background/aims:
Malathion is a pesticide of the organophosphate class widely used since the 1980's, and in Brazil it has been used in the control of the Aedes aegypt mosquito. Children and teenagers of rural populations and others living in areas where malathion is used are frequently exposed to this compound. Considering the toxic effects of malation exposure during peripuberty to the male and female reproductive systems, the aim of this study was to evaluate if malathion exposure during the peripubertal periods later impairs placentation and fetal development in female Wistar rats.

Methods:
Wistar rats were exposed to 10 (M10) or 50 (M50) mg/kg of malathion diluted in saline via gavage daily from PND 22 to 60. Starting at PND61, females were submitted to a mating protocol. Pregnancy was detected by the presence of spermatozoa in the vaginal smear (GD0). At GD 18, dams were euthanized, the fetuses and placentas were harvested, measured and weighted. The glycogen reserves in placenta were dosed and placental fetal capillaries were measured in the labyrinth. Placental oxidative profile was evaluated. The experimental protocol approved by the Ethics Committee for the Use of Animals in Research (OF. CIRC. CEUA 17/2023).

Results:
Fetuses in M10 and M50 were smaller ($p=0.0008$; $p=0.001$, respectively) and the fetal/placental weight ratio was increased in M10 ($p=0.0264$). Glycogen reserves were diminished (0.0155) and the fetal capillaries were enlarged ($p<0.0001$) in the placentas of M10. Lipid peroxidation ($p=0.0191$) and reduction in total glutathione concentration ($p=0.0011$) were found in M50, SOD ($p=0.0031$) and GST ($p=0.0005$) activities and total glutathione concentration ($p<0.0001$) were reduced in M10.

Conclusions:
Pre-conceptional exposure to low doses of malathion impaired placentation and the offspring's fetal growth in Wistar rats, through mechanisms associated to oxidative stress and alterations in fetal circulation – leading to early depletion of placental glycogen reserves.

Funding:
Partially funded by CAPES (Funding Code 001) and CNPq (process 313704/2021-0).

Key-words: (up to 5):
oxidative profile, placenta, organophosphate, intrauterine development, reproductive toxicity

Abstract #00005662 en

Maternal High-Sugar Diet Programs Sex-Specific Risk of MASLD in Offspring.

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Brito Camila (1), Pontes Jaqueline (1), Macedo Bruno (1), Silva Odara (1), Sanches Jonas (1), Freitas Perla (1), Flister Karla (1), França Lucas (1), Pinto Bruno (1), Paes Antonio Marcus (1)
(1) Federal University of Maranhão

Background/aims:
A metabolically unbalanced intrauterine environment increases the risk of chronic non-communicable diseases later in life. This study investigated whether early Metabolic Associated Steatotic Liver Disease (MASLD) onset occurs in the offspring of rats exposed to a high-sucrose diet (HSD) during the perigestational period.

Methods:
Female rats were fed an isocaloric HSD (25% sucrose) or regular chow (10% sucrose, CTR) from preconception through lactation. Male and female offspring (n=5–8/group/sex) were fed regular chow from weaning until euthanasia at 30 or 90 days of age (d.o.), when blood and metabolically relevant tissue samples were collected for further analysis (CEUA/UFMA 23115.002915/2023-62).

Results:
HSD dams exhibited increased body weight from preconception (+9.7%, $p<0.01$) through gestation (+6.5%, $p<0.05$) and lactation (+4.1%, $p<0.05$). Compared to CTR dams, HSD mothers showed higher serum triglycerides (+95.5%, $p<0.05$), impaired glucose tolerance (+29.7%, $p<0.01$), and elevated TyG index post-lactation (+9.7%, $p<0.05$), without histological alterations in the liver. HSD offspring displayed greater weight gain during lactation (+12.1%, $p<0.001$), which persisted in males up to 90 d.o. In HSD males, early metabolic dysfunction (increased triglycerides and insulin resistance) was evident at 30 d.o. and worsened by 90 d.o. Females exhibited transient fasting hyperglycemia and hepatic lipid accumulation at 30 d.o., which attenuated in adulthood. While steatosis was present in both sexes at 30 d.o., it worsened in males by 179.9% ($p<0.01$) at 90 d.o. HSD females demonstrated FASN gene overexpression at both time points, with upregulation of PPAR-γ, PGC1α, and PPARα only at 90 d.o. No significant changes in lipogenesis gene expression were detected in HSD males.

Conclusions:
These findings highlight the need for early monitoring of metabolic markers in offspring of metabolically compromised mothers and reveal a clear sex-specific susceptibility to the onset and progression of MASLD.

Funding:
CNPq, CAPES and FAPEMA

Key-words: (up to 5):
Added sugars; Fetal programming, intergenerational outcomes; NAFLD.

Abstract #00005663 en

Small litter size mitigates high-sucrose-induced liver oxidative stress

Role of Infant and Young Child Feeding Practices on Long-Term Health

Martins de Andrade Fagundes Miliane (1), Letícia Silva Juliana (1), Jesus de Deus Isabela (1), Rezende Ribeiro de Abreu Aline (1), Silveira Breguez Gustavo (2), Antunes Silva Ângela (3), Cristina da Silva Oliveira Siqueira Érika (3), Martins Carneiro Cláudia (4), Barbosa de Queiroz Karina (1)
(1) Laboratory of Experimental Nutrition, Federal University of Ouro Preto, (2) Lab. Nutritional Biochemistry and Molecular Biology, Federal University of Ouro Preto, (3) Animal Science Center, Federal University of Ouro Preto, (4) Laboratory of Immunopathology, Federal University of Ouro Preto

Background/aims:
The DOHaD concept suggests that perinatal exposures modulate the health-disease process. Metabolic imprinting (MI) induced by the small litter size (SL) model is widely used but yields controversial results. Postnatal exposure to deleterious diets, such as a high-sucrose diet (HSD), promotes oxidative stress, a risk factor for liver diseases. We investigated whether MI induced by SL affects the hepatic oxidative balance altered by HSD in young rats.

Methods:
Ethics Committee Approval Protocol: 2245040518. Wistar rats (P0, n=32) were divided into control litter (CL; 8 pups/dam) and small litter (SL; 4 pups/dam). After weaning, they were fed either a standard commercial diet (STD) or a high-sucrose diet (HSD; 30% sucrose) for 8 weeks, forming four groups: (i) STD-CL (n=8); (ii) HSD-CL (n=8); (iii) STD-SL (n=8); (iv) HSD-SL (n=8). After euthanasia, the liver was collected for analysis.

Results:
Superoxide dismutase (SOD) and catalase (CAT) enzymatic activities were affected by the interaction between variables ($P<0.05$), with a 31.6% reduction in SOD activity in the HSD-SL group compared to STD-SL, and a 28.2% reduction compared to HSD-CL. CAT activity was reduced by 34.8% in the HSD-SL group compared to the STD-SL group, and by 36.3% compared to the HSD-CL group. Sulfhydryl groups decreased by 28.6% due to the influence of the post-weaning diet ($P<0.05$) in the HSD-SL group compared to the STD-SL group. Carbonyl protein (PCO) increased by 43.9% in HSD-CL compared to STD-CL and decreased by 28.1% in HSD-SL relative to HSD-CL. Similarly, malondialdehyde (MDA) levels were 43.1% higher in HSD-CL than in STD-CL and 34.7% lower in HSD-SL compared to HSD-CL.

Conclusions:
MI induced by SL reduces antioxidant enzyme activities and attenuates oxidative damage induced by HSD consumption.

Funding:
This study was financed by CAPES code 001, FAPEMIG APQ-02200-21 e APQ – 04983-22, PDPG-III FAPEMIG_CAPES, CCA-UFOP, and UFOP.

Key-words: (up to 5):
metabolic imprinting; small litter size; high-sucrose diet; oxidative stress, liver.

Abstract #00005664 en

Repercussions of maternal high-fat/high-caloric diet associated with daily resistance training on serotonin and kynurenine pathways in fetal brain

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Da Silva Aragao Raquel (1), Oliveira Débora Kathuly da Silva (1), Lima-Oliveira Débora Priscila (1), Chaves Wenicios Ferreira (2), Melo Kellyanne Rafaella de Oliveira (1), Nelo Sarah Rachel de Barros (1), da Silva Luis Henrique Facunde (1), Alves-Neto Josias Gomes (1), do Nascimento Evelly Talita (1), Torsoni Marcio Alberto (2), Antonio-Santos Jose (1) (1) Universidade Federal de Pernambuco, (2) Universidade Estadual de Campinas

Background/aims:
Aims: to evaluate the neurotrophic factor and genes of the serotonin and kynurenine pathway expression in the brains of fetuses whose mothers performed high-intensity resistance training associated with a high-fat/high-calorie diet.

Methods:
Methods: Female Wistar rats received control (CD, 3.6 kcal/g, 10% fat) or a high-fat/high-caloric diet (HFD, 4.7 kcal/g, 47% fat, mainly from lard) for 3 weeks before mating until the 20th gestational day. During the same period, rats performed resistance training consisting of 7 to 9 stair climbs at 80% of the maximum carrying capacity, 5 days/week (T) or remained untrained (U). Four groups were formed: CD-U, CD-T, HFD-U, HFD-T, n=4-6 for all groups. Euthanasia occurred on the 20th gestational day, and the fetal brain was collected. Ethical approval 105/2021.

Results:
Results: In the brains of male fetuses, Bdnf mRNA expression was reduced in HFD-U and CD-T compared to CD-U ($p=0.0146$, $p=0.0004$, respectively). Tph2 expression was increased in HFD-U and CD-T compared to CD-U ($p=0.0018$, $p=0.0338$, respectively). Maoa expression was reduced in both trained groups compared to the untrained groups (CD-T vs. CD-U $p=0.0028$, HFD-T vs. HFD-U $p=0.0034$). Htr2a expression was increased in CD-T compared to CD-U ($p=0.0012$) and decreased in HFD-T compared to CD-T ($p<0.0001$). Ido1 expression was increased in HFD-U and CD-T compared to CD-U ($p=0.0015$, $p=0.0009$, respectively). Kat2 expression was increased in HFD-T compared to CD-U ($p=0.035$). In the brains of female fetuses, differences were only observed in Bdnf and Htr1a expression, where the HFD-T group had decreased expression compared to HFD-U for both genes ($p=0.0085$, $p=0.011$, respectively).

Conclusions:
Conclusions: The maternal diet and resistance training impacted the male fetal brain more significantly than the female fetal brain. The serotonin pathway was altered in both male and female fetuses, while the kynurenine pathway was modified solely in the male fetal brain.

Funding:
Funding: CAPES code 001-PROAP/PPGN/PROPG/CAPES 2024, APQ-1062-4.05/22, UFPE 23076.038106/2024-72.

Key-words: (up to 5):
Kynurenine, Maternal diet, Pregnancy, Serotonin, Strength exercise

Abstract #00005666 en

Daycare as a Protective Factor Against Obesity in Children Under 5 Years Old

Role of Infant and Young Child Feeding Practices on Long-Term Health

Lima Gyovana Lara (1), Souza Fabíola Isabel (1), Schoeps Denise (1), Sarni Roseli (1), Filipini Rosângela (1), Leite Narjara (1), Cavalcante Guilherme (2), Moraes Simone (1)
(1) Centro Universitário Faculdade de Medicina do ABC, (2) Faculdade de Medicina da Universidade de São Paulo

Background/aims:
The significant increase in obesity in the pediatric age group is related to exposure to an obesogenic environment. This study assessed the association between risk factors and overweight in children under 5 years of age.

Methods:
A cross-sectional, controlled study was carried out with 140 children under 5 years of age enrolled in day-care centers in the municipality of Santo André. Family history, dietary intake and anthropometry (weight and height) were assessed to calculate anthropometric indicators. The study was approved by the Research Ethics Committee of the FMABC University Center, protocol no. 75478423.2.0000.0082.

Results:
In the population evaluated, 27 children (19.3%) were overweight. Some form of breastfeeding was reported in 122 children (88.4%), of whom 31 (26.0%) were exclusively breastfed for up to 4 months and 27 (23.08%) were breastfed for less than 6 months. The use of infant formula was reported in 90 (65.2%) children. With regard to eating outside daycare centers, 98 (75.9%), 90 (68.7%) and 111 (84.7%) reported high consumption of sweets, high-fat foods and sugary drinks, respectively. The variables studied were not significantly associated with overweight and obesity in the children assessed, even when stratified into those under 24 months and those between 24 and 60 months.

Conclusions:
In this study, the classic risk factors were not associated with overweight in children under 5 years old. The shared environment in the nursery school for most of the day may have been the protective factor for overweight in this age group - whether through adequate school meals, a safe environment for playing and physical activity, or the inclusion in the curriculum content linked to health promotion and an appropriate lifestyle for children and their families in an integrated way.

Funding:
Own.

Key-words: (up to 5):
Childhood obesity, nutrition, pre-school.

Abstract #00005668 en

Early human morphologic development in 3D Virtual Reality and fetal growth and birth outcomes: The Generation R Next Study

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Graafland Naomi (1), Posthumus Anke (1), Mulders Annemarie (1), Gaillard Romy (1), Koning Anton (1), Jaddoe Vincent (1), Steegers Eric (1), Rousian Melek (1)
(1) Erasmus MC

Background/aims:
Adverse birth outcomes such as small-for-gestational-age (SGA), low birth weight, and preterm birth are linked to increased long-term health risks. While early fetal growth has been associated with these outcomes, the role of embryonic morphologic development in influencing these outcomes remains less well understood. We aimed to investigate the associations of embryonic morphologic development and growth trajectories with fetal growth and birth outcomes.

Methods:
966 spontaneous singleton pregnancies were enrolled from the Generation R Next Study, a population-based prospective cohort in the Netherlands, and underwent 3D transvaginal ultrasound measurements before 10+3 weeks of gestation. Embryonic morphological development (Carnegie Stages) and growth (crown-rump length) were assessed at 7 and 9 weeks of gestation using virtual reality techniques. Individual developmental and growth trajectories were modeled using linear mixed models. Associations with third-trimester estimated fetal weight (EFW), birth weight, and risk of SGA, low birth weight, and preterm birth were examined using linear and logistic regression analyses.

Results:
Accelerated embryonic development and growth were both positively associated with third-trimester estimated fetal weight (EFW) (β: 0.40, 95% CI: 0.33–0.46 and β: 0.14, 95% CI: 0.12–0.17, respectively) and birth weight (β: 0.19, 95% CI: 0.12–0.26 and β: 0.08, 95% CI: 0.06–0.10, respectively) z-scores. Delayed embryonic morphologic development and growth (lowest 20%) was associated with increased odds of being born SGA (OR: 2.00, 95% CI: 1.27–3.14 and OR: 1.63, 95% CI: 1.03–2.57], respectively). No significant associations were observed with preterm birth or low birth weight.

Conclusions:
Embryonic development and growth are positively associated with fetal growth and birth weight. Delayed embryonic development and embryonic growth restriction increase the risk of being born SGA. These findings highlight the potential for early identification of at-risk pregnancies, offering opportunities for timely intervention to improve perinatal outcomes.

Funding:
This research was supported by the Erasmus MC, ZonMw, and the Netherlands Organization for Scientific Research (NWO).

Key-words: (up to 5):
Carnegie Stages, Crown-rump length, embryonic period, Small-for-gestational-age, Birth outcomes

Abstract #00005670 en

Nutrient Intake and Plasma Levels in Pregnancies Undergoing Intrauterine Repair Surgery for Spina Bifida

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Uribe-Cerda Sofia (1), Arias Andreina (2), Peñailillo Reyna (2), Romo Patricia (2), Valdebenito Patricia (3), Figueroa Horacio (4), Moyano Felipe (5), Yamamoto Masami (4), Busso Dolores (2)
(1) Universidad Andrés Bello, (2) Universidad de los Andes, (3) IMPACT, Center of Interventional Medicine for Precision and Advanced Cellular Therapy, (4) Department of Obstetrics and Gynecology, Clínica Universidad de los Andes, (5) Department of Surgery, Clínica Universidad de los Andes

Background/aims:
Spina bifida (SB) is a congenital malformation that causes lifelong disabilities. Folate is critical in SB prevention, and preconceptional folic acid supplementation is an established measure. We assessed nutrient intake and plasma levels in a cohort of Chilean women undergoing intrauterine SB repair.

Methods:
Pregnant women (week 18-28) undergoing intrauterine SB repair at Clínica Universidad de los Andes (n=6) were recruited. Controls were women undergoing fetal surgery for other malformations (n=7). Written informed consent was obtained; the Ethics Committee of U. Andes approved this study (CEC2024031). Plasma levels of lipids, vitamins B12, E, D, C, and homocysteine were determined using standard clinical methods. Dietary intake was evaluated by trained nutritionists using two non-consecutive 24-hour recalls and analyzed with Food Processor®. Outcomes were compared by Mann-Whitney.

Results:
Women in the SB group showed a tendency toward higher saturated fat (p=0.06) and cholesterol (p=0.11) intake, and higher circulating lipids (p=0.036). A trend for lower vitamin C intake (p=0.06) and plasma concentration (p=0.07) was observed in the SB group. Vitamin B12 intake was higher in the SB group (p=0.03), although plasma levels were similar between groups. Folate, vitamin D, and E were consumed below the estimated average requirement (EAR) for pregnant women in both groups, yet plasma levels remained within normal ranges. Homocysteine levels were comparable and below recommended thresholds (10 μm/L).

Conclusions:
SB pregnancies were associated with higher lipid intake and levels, and lower vitamin C intake and plasma concentrations. Discrepancies between dietary intake and plasma biomarkers were noted for several nutrients, including folate and B12. These findings highlight the need to assess both dietary intake and biochemical status when evaluating maternal nutrition and suggest that nutritional factors beyond folate may contribute to SB risk.

Funding:
ANID—Basal funding for Scientific and Technological Center of Excellence, IMPACT, #FB210024 and ANID-Fondecyt 1221376 (to D.B.)

Key-words: (up to 5):

spina bifida, maternal nutrition, micronutrients

Abstract #00005672 en

Gene expression of the insulin signaling pathway in pancreatic islet cells of diabetic rats and offsprings of diabetic rats

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Picolo Gomes Maria Eduarda (1), Gonçalves Paula Verônyca (2), Quintanilha Gallego Souza Franciane (2), Soares Barco Vinícius (2), Rocha de Souza Maysa (2), Volpato Gustavo Tadeu (3), Damasceno Débora Cristina (2)
(1) São Paulo State University , (2) Botucatu Medical School, São Paulo State University (Unesp), (3) Institute of Biological and Health Sciences, Federal University of Mato Grosso (UFMT)

Background/aims:
Diabetes mellitus (DM) presents a serious threat to public health and the economy. In 2024, global costs exceeded one trillion dollars, according to the International Diabetes Federation (IDF), and are expected to keep rising. Type 2 DM (DM2) is the most prevalent class, which has several repercussions and can affect offspring by promoting glucose intolerance, insulin resistance, and abnormal gene expression profiles related to insulin signaling. Therefore, the identification of the differentially expressed genes to study and understand the pathophysiological mechanisms involved in the repercussions on pancreatic islets of offspring using an experimental mode is relevant. In our study, we aimed to analyze the gene expression profile of the insulin signaling pathway in pancreatic islets from diabetic rats and offspring of diabetic rats.

Methods:
The Local Ethics Committee for Animal Use (#1461/2024) approved all the protocols. Female Sprague-Dawley rats neonatally received a beta-cytotoxic drug (streptozotocin - Dm group) or Vehicle (citrate buffer - Control group). In adulthood (120 days), after diabetes confirmation, they were mated to obtain offspring (ODm group). All adult animals (n=3/group) were euthanized for a collection of the pancreas to isolate pancreatic. RNA was extracted and analyzed by microarray using Transcriptome Analysis Console (TAC). $P<0.05$ was a statistically significant level.

Results:
The differentially expressed genes (DEGs: GSK3B, PPP1CB, and CALM1 of the Dm versus Control, and ODm versus Control comparisons were upregulated, while these genes were downregulated in the ODm versus Dm comparison. These DEGs are related to the PI3K/AKT axis which is an axis of the insulin signaling pathway responsible for glucose uptake.

Conclusions:
Gene expression analysis indicates abnormal genes in insulin signaling in diabetic rats and the Offspring of diabetic rats, suggesting an intergenerational impact of maternal diabetes on gene regulation and glucose uptake.

Funding:
PROPG/PROPe (05/2022), FAPESP (Process Number 2023/04866-4).

Key-words: (up to 5):
diabetes, endocrine pancreas, gene expression, fetal programming, rats.

Abstract #00005676 en

Maternal obesity induces sex-specific alterations on gut microbiota correlated with fecal levels of endocannabinoid-like molecules in weanling rat offspring

Mechanisms Determining Transgenerational Effects of Health and Disease

Macedo de Almeida Mariana (1), Calvino Camila (2), Fonseca Reis-Gomes Clara (2), Ávila Alpino Gabriela de Cássia (3), Almeida Brasiel Poliana Guiomar (3), Dutra Medeiros Julliane (4), Potente Dutra Luquetti Sheila Cristina (3), Pazos-Moura Carmen (2), Trevenzoli Isis Hara (2)

(1) Departamento de Farmacologia, Universidade Federal de Juiz de Fora (UFJF), (2) Instituto de Biofísica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro (UFRJ), (3) Departamento de Nutrição, Universidade Federal de Juiz de Fora (UFJF), (4) Departamento de Biologia, Universidade Federal de Juiz de Fora (UFJF)

Background/aims:

Maternal obesity increases adiposity and glucose intolerance in weanling rat offspring with increased gut endocannabinoid signaling. This phenotype was associated with reduced gut permeability, suggesting an adaptative response of the immature intestine. Maternal obesity also decreases fecal excretion of the endocannabinoid-like molecules, oleoylethanolamide (OEA) and palmitoylethanolamide (PEA), which have anti-inflammatory effects and decrease gut permeability. However, the associations between gut microbiota and the fecal levels of endocannabinoid-like molecules are mostly unknown. We aimed to explore whether the effect of maternal obesity on the gut microbiota is correlated with fecal levels of PEA and OEA in the offspring.

Methods:

Female Wistar rats received a control diet (C; 11% fat, n=10) or an obesogenic diet (OD; 40% fat + 9.5% sucrose, n=10) nine weeks prior mating, and during gestation and lactation (ethical approval n. 129/21, UFRJ). At weaning, fecal samples were collected of male and female offspring for analysis of microbiota composition by sequencing 16S rRNA bacterial gene (V3-V4 region). Amplicon Sequence Variants (ASV) were obtained through DADA2 pipeline. The differentially abundant ASVs were identified using DESeq2. Correlations between microbial composition and fecal levels of PEA and OEA were identified using Spearman's correlation.

Results:

Only in male offspring, maternal obesity decreased the abundance of Mucispirillum ($p<0.0001$) while increased abundance of Blautia ($p<0.0001$). Mucispirillum was positively correlated with fecal levels of PEA ($r = 0.56$, $p = 0.05$) and OEA ($r= 0.52$, $p= 0.05$), while Blautia was negatively correlated with fecal levels of PEA ($r = -0.55$, $p = 0.05$) and OEA ($r = 0.48$, $p = 0.06$), which could contribute to low fecal levels of endocannabinoid-like molecules in OD males.

Conclusions:

There was a sex-specific cross talking between gut microbiota and the endocannabinoid-like molecules during maternal obesity. Fecal levels of PEA and OEA could be noninvasive biomarkers of gut dysbiosis in male offspring rats.

Funding:

FAPERJ, FAPEMIG

Key-words: (up to 5):

Maternal obesity, high-fat high-sugar diet, gut microbiota, endocannabinoid-like molecules

Abstract #00005682 en

Impact of Maternal Overweight and Butyrate Treatment in Colon Inflammation

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Dechamps Victoria (1), Labiano Marina (1), Flores Quiroga Jeremías Pablo (1), Heinecke Maria Florencia (1), Galarza Rocío (2), White Verónica (1)
(1) CEFyBO - CONICET - UBA, (2) CEREGGeo-FCyT-UADER

Background/aims:
We previously observed that the fetuses and offspring from overweight rats display increased intestinal permeability with decreased expression of tight junction proteins and increased protein levels of pro-inflammatory cytokines in small intestine. Butyrate is a short chain fatty acid product of fiber metabolism from intestinal microbiota that improves lipid metabolism and prevents inflammation. Maternal oral administration of butyrate prevented offspring lipid impairments. Our aim was to evaluate whether maternal overweight disturbed cytokine and tight junction levels related to epithelial barrier function and whether maternal butyrate treatment is able to restore them.

Methods:
Female Wistar rats were fed standard (CT rats) or high saturated fat (FD rats) chow for 8 weeks and mated with CT males. Butyrate (3%) or vehicle was orally administered daily during gestation and 3 days per week during lactation (FDB rats). Mothers were euthanized after weaning and the offspring were euthanized at 140 days of age. The offspring were fed a control diet. Offspring colon mRNA levels were assessed by RT-qPCR and proteins by western-blot and plasma interleukin 1-β (Il-1β) by EIA.

Results:
The offspring from FD rats showed increased circulating levels of Il1 (57%, p≤0.05). Colon mRNA levels of Il18 were increased (16% p≤0.05) and TNF decreased (32.1% p≤0.05) in male offspring from FD rats. FDB male offspring showed decreased levels of Il10 compared to CT (51.3% p≤0.05) and FD (23.5% p≤0.05) offspring respectively. Also, occludin a protein involved in tight junctions resulted decreased in both female (20% p≤0.05) and male (10% p≤0.05) FD offspring and restored by maternal butyrate treatment

Conclusions:
Maternal overweight programs a pro-inflammatory environment and epithelial barrier-linked disturbances in the offspring with sex-dependent differences. Maternal treatment with butyrate restored most of the values and might be protective for the colonic barrier function of the offspring from overweight rats

Funding:
PICT-2020-Serie-A-nº-01125/ PICT-2021-nº-I-A-00381-PIP 2022/2024 CONICET. Ethical Approval: CICUAL-n°3001-2022. The authors state that they have no conflicts of interest

Key-words: (up to 5):
Maternal overweight-intestine barrier function-butyrate intervention-programming

Abstract #00005685 en

Melatonin reverts gestational hypoxia-induced vascular dysfunction in carotid arteries of guinea pigs

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Herrera Emilio (1), Paz Adolfo (1), Navarrete Álvaro (2), Catrilef-Pozo Cristian (2), Jorquera Sofía (1), Herrera Pedro (1), Yañez Aldo (1), Astorga Cristian (1), Jimenez Tamara (1), Beñaldo Felipe (1)
(1) Universidad de Chile, (2) Universidad de Santiago de Chile

Background/aims:
Gestational hypoxia (GH) increases cardiovascular disease susceptibility during adulthood and is associated with oxidative stress-induced vascular dysfunction. We proposed that an antioxidant melatonin treatment counteract the GH-induced vascular dysfunction in carotid arteries of guinea pigs.

Methods:
All procedures were approved by the Bioethical Committee (20354-MED-UCH). Pregnant guinea pigs were exposed to either normoxia (720 torr, Nx) or hypoxia (470 torr, Hx) and treated with melatonin (Mel, 1mg/Kg daily) or vehicle from gestational day 30 until term (~70 days). After birth, the litter returned to normoxic conditions. Carotid blood flow velocities (maximum [Vmax] and mean [Vmean]) were assessed via ultrasound during one-postnatal year. Juveniles (2,5 months old; n=6 per group) and adults (1 year old; n=12 per group) were euthanized, and their carotid arteries were dissected. Vasoreactivity was evaluated using wire-myography (K^+-induced contraction, sodium nitroprusside [SNP] for endothelium-independent relaxation, and methacholine for endothelium-dependent relaxation). Ring-opening and axial stress tests evaluated biomechanical properties (opening angle and elastic modulus). Structural composition (elastin, collagen, and nuclear density) was assessed by histology. Data was analyzed by F-test or Two-Way ANOVA ($p \leq 0.05$).

Results:
GH consistently increased heart rate and Vmean values throughout adulthood. In juvenile animals, GH reduced K+ maximal contraction as increased endothelial-dependent vasodilation, where the latter effect was reverted by melatonin treatment. Interestingly, neither GH nor melatonin affected carotid structure. However, GH reduced nuclei density in both life stages, this effect was reverted by melatonin in juvenile animals. Moreover, elastin bands were increased in Hx adults. However, this was associated with a reduced elastin tortuosity index. These effects were related to a GH-induced increased initial elastic modulus and decreased stretch ratio. Importantly, melatonin increased elastin deposition in Hx adults, associated with increased cauchy stress.

Conclusions:
Melatonin reverses GH-induced vascular dysfunction by improving reactivity and biomechanics, potentially through oxidative stress reduction. Still, further mechanistic studies are needed.

Funding:
Doctoral Fellowship ANID 21230893 and Master Fellowship ANID 22251441, supported by FONDECYT Regular 1241502.

Key-words: (up to 5):

Antioxidant treatment, Vascular dysfunction, Intrauterine hypoxia, Systemic arteries, Brain-Sparing effect

Abstract #00005691 en

Intrauterine Exposure to Maternal Obesity Accelerates Developmental Adipogenesis and Leads to Later-life Progenitor Exhaustion.

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Scheidl Taylor (1), Yonan Sophie (1), Wager Jessica (1), Thompson Jennifer (1)
(1) University of Calgary

Background/aims:
Two distinct pools of adipose progenitor cells (APCs) are established in utero. Developmental APCs give rise to adipocytes during early establishment of adipose depots, while APCs residing in adult depots can be stimulated to differentiate and maintain the functional integrity of adipose tissue. We determined how intrauterine exposure to maternal obesity impacts APC abundance and function.

Methods:
Offspring (Off) born to obese (Ob) dams fed a high fat/high fructose diet (HFD) were compared to offspring born to lean (Ln) dams fed a low-fat diet (LFD). After puberty, offspring were randomized to HFD, LFD or treatment with rosiglitazone (Rosi). Fat mass was determined using TD-NMR and serum adipokines measured by multiplex immunoassay. Flow cytometry quantified APC and macrophages, while single cell RNA sequencing provided in-depth information on APC subtypes. Isolated APCs were assessed for adipogenic competency in vitro.

Results:
After birth (PND10), subcutaneous adipose depots of Ob-Off vs. Ln-Off were comprised of larger adipocytes and a greater number of CD34+/PDGFRα+ APCs ($p<0.05$). Single cell sequencing unveiled two trajectories of APCs at PND10 expressing markers consistent with other studies. Lineage clusters expressing markers of committed preadipocytes appeared to be less abundant in Ob-Off. At PND35, APCs isolated from Ob-Off exhibited greater adipogenic competency and lower proliferative capacity ($p<0.05$) and whole-body fat mass was higher. However, the pubertal accumulation of body fat from PND21-PND35 was virtually absent in Off-Ob ($p<0.0001$). After puberty, Ob-Off fed LFD had lower abundance of CD34+/PDGFRα+ APCs vs. Ln-Off ($p<0.05$) and were more susceptible to HFD-induced obesity ($p<0.0001$). Off-Ob on HFD were hyper-insulinemic ($p<0.01$) and hyperglycemic ($p=0.06$) and had more M1-like macrophages ($p=0.05$) Pharmacological stimulation of adipogenesis by Rosi led to greater fat accumulation ($p<0.01$) and decreased APC abundance ($p<0.05$) in Ob-Off.

Conclusions:
Perturbed developmental adipogenesis in offspring born to obese dams may predispose to APC exhaustion and adipose dysfunction.

Funding:
PJT - 162452

Key-words: (up to 5):
obesity, adipose tissue, maternal programming, development

Abstract #00005693 en

Pre-Gestational Exercise Alleviates Prenatal Stress-Induced Neonatal Behavioral and Hepatic Alterations

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Potter Spagnol Hérika Raquel (1), Luft Carolina (1), Severo da Costa Mariana (1), Rodrigues de Oliveira Jarbas (1), Fagundes Donadio Marcio Vinicius (2)
(1) PUCRS, (2) PUCRS and UIC

Background/aims:
Prenatal stress (PNS) disrupts offspring development, impairing neonatal behavior and hepatic function, potentially increasing long-term health risks. Pre-gestational maternal exercise may counteract these effects, promoting resilience. This study examines the protective role of pre-gestational exercise against PNS-induced changes in female BALB/c mice, aligning with One Health by addressing intergenerational health. In this study, we aimed to evaluate whether maternal physical exercise before gestation mitigates PNS-induced impairments in neonatal behavior and hepatic alterations in female offspring at 10 days of life (PND10).

Methods:
Female BALB/c mice were divided into three groups (Ethics Committee #8465): control (CON), prenatal stress (PNS), and pre-gestational exercise + PNS (EX+PNS). Nest seeking behavior was evaluated on PND9. On PND10, livers were collected to measure cholesterol, glucose, triglycerides, oxidative stress markers (catalase, TBARS, DCF, GSH), and inflammatory markers (TNF-α, IL-6).

Results:
PNS offspring exhibited increased latency in nest seeking behavior, indicating impaired olfactory-guided navigation, which was prevented by pre-gestational exercise ($p<0.05$). In the liver tissue, PNS reduced triglycerides, while EX+PNS group showed increased serum glucose compared to PNS group ($p<0.05$). PNS group showed elevated hepatic catalase and TBARS compared to CON and EX+PNS groups ($p<0.05$), reflecting oxidative stress. Conversely, PNS decreased hepatic DCF and GSH, effects absent in the EX+PNS group ($p<0.05$). PNS increased hepatic TNF-α gene expression compared to CON group ($p<0.05$), promoting inflammation, which pregestational exercise prevented ($p<0.05$). Hepatic IL-6 gene expression were significantly reduced in both PNS and EX+PNS groups, when compared to CON group ($p<0.05$), suggesting a complex inflammatory response.

Conclusions:
Pre-gestational exercise ameliorates PNS-induced impairments in neonatal nest seeking behavior and hepatic function in female offspring, reducing oxidative and inflammatory changes. These findings highlight the role of maternal exercise in mitigating early-life stress effects, with implications for intergenerational health strategies and policies.

Funding:
Coordenação de Aperfeiçoamento de Pessoal de Nivel Superior – Brasil (CAPES) – Finance Code 001.

Key-words: (up to 5):
Nest Seeking Behavior, Oxidative Stress, Inflammation

Abstract #00005696 en

Study of COVID-19 effects on pregnancy and the mechanisms associated with placental vascular dysfunction.

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Urrea Susan (1), Benavente Noelia (1), Aguilera Claudia (1), Contreras Vicente (1), Córdova Claudio (2), San Martín Sebastián (2), Cisterna Marjorie (1), González-Ortiz Marcelo (1)
(1) Laboratorio de Investigación Materno-Fetal (LIMaF), Universidad de Concepción, (2) Centro de Investigaciones Biomédicas, Universidad de Valparaíso

Background/aims:
SARS-CoV-2 infection and the COVID-19 pandemic increased the risk of preterm birth and obstetrical adverse outcomes. The large-conductance calcium-activated potassium channels (BKCa) are highly relevant for placental vascular function, and oxidative stress and inflammation could be increased by SARS-CoV-2 infection. This study aimed to determine the BKCa expression and placental alterations in COVID-19 cases.

Methods:
Placental samples from pregnant women with positive or negative tests for SARS-CoV-2 were obtained during the COVID-19 pandemic (Approved by the Ethics committee of Concepcion Health Service, CEC-SSC 20-11-60). Tissue microarray samples stained with H/E for structure observation and immunohistochemistry for NADPH oxidase 4, eNOS and CD68 were analyzed. Total RNA was isolated, and RT-PCR for BKCa α, β1, β2, and β3 subunits and 28S was performed. The BKCa subunit/28S relation was analyzed by Image J and GraphPad Prism software. The Mann–Whitney U and Kruskal–Wallis tests were applied for statistical analysis.

Results:
Histological observations revealed CD68-positive cells, significant alterations in the vasculo-syncytial membranes, and higher expression of NADPH oxidase 4 and eNOS in severe COVID-19 cases. BKCa α subunit mRNA was increased by 3.0±0.8-fold, particularly in the chorionic plate of severe cases. No differences were observed in the mRNA of BKCa β1-β3 subunits in the chorionic plate. In the chorionic villi, no statistically significant differences existed in the mRNA levels of BKCa subunits.

Conclusions:
Alterations in BKCa expression in COVID-19 cases are correlated with placental inflammation and oxidative stress in the placenta. The decrease in vasculo-syncytial membranes could be related to placental insufficiency. We propose that BKCa is part of a compensatory mechanism in response to the vascular injury in severe COVID-19 cases.

Funding:
FONDECYT Regular 1241905 (ANID, Chile)

Key-words: (up to 5):
BKCa, placenta, COVID-19, oxidative stress, inflammation

Abstract #00005697 en

Impact of Prenatal Nicotine Exposure on Adult Female Mice Offspring Memory and Learning

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Stocchero Bruna (1), Luft Carolina (1), Kaiber Daniela (1), Viola Thiago (1)
(1) PUCRS

Background/aims:
Smoking poses severe risks during pregnancy. Prenatal nicotine exposure, a key tobacco component, can cause miscarriage, preterm birth, and cognitive deficits in offspring. Female offspring may face heightened neurodevelopmental risks, yet sex-specific effects are understudied. This study examines how prenatal nicotine exposure impacts spatial learning and memory in adult female mice offspring using the Barnes Maze.

Methods:
Pregnant Balb/CJ female mice received 50 µg/mL nicotine ditartrate (in 2% sucrose water, pH 7.8) or sucrose-only control solution during gestation (Ethics Committee #11698). Adult female offspring underwent Barnes Maze testing on a 92-cm platform with 20 holes, using light and noise as aversive stimuli. Following three-day habituation, mice completed five days of training (three 3-min trials/day) and a 1.5-min probe trial, assessing latency, errors, and success rate. A blinded experimenter recorded outcomes.

Results:
A generalized linear mixed model showed that Control mice had a higher overall success rate during training than Nicotine-treated mice ($p < 0.001$), with significant group differences across days ($p < 0.001$) and within-day trials ($p < 0.001$), particularly on Day 4 ($p < 0.001$). On the Day 4 to Day 5 transition, Control mice showed increased error (77.8% vs. 25.0%; $\chi^2(1) = 5.743$, $p = 0.017$) and latency improvement (77.8% vs. 33.3%; $\chi^2(1) = 4.073$, $p = 0.044$). In the probe trial, Control mice had a higher success rate (77.8% vs. 50.0%), though not significant ($\chi^2(1) = 1.683$, $p = 0.195$).

Conclusions:
Control mice outperformed Nicotine-treated mice in training success and memory retention, particularly on Day 4, suggesting nicotine-induced impairments in learning and memory consolidation. We will continue this research by increasing the sample size and conducting molecular analysis with hippocampus tissue to confirm these findings and explore underlying mechanisms.

Funding:
Coordenação de Aperfeiçoamento de Pessoal de Nivel Superior – Brasil (CAPES) – Finance Code 001

Key-words: (up to 5):
Neurodevelopment, Nicotine Exposure, Memory

Abstract #00005699 en

Impact of maternal psychosocial conditions in different gestational clinical situations on the behavior of their children at pre-school age

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Salazar Viviane (1), Zanella Batistello Camila (1), Rombaldi Bernardi Juliana (1), Valentini Nadia Cristina (1), Homrich da Silva Clécio (1), Zubaran Goldani Marcelo (1), Ruschel Bandeira Denise (1)
(1) Universidade Federal do Rio Grande do Sul

Background/aims:
Maternal mental health is a critical factor influencing child development. Between 12% and 20% of women may experience mental disorders during pregnancy or postpartum, while gestational complications affect 17% to 23% of pregnancies. These conditions can create an unfavorable environment for child development, particularly during early childhood. This study aimed to analyze the impact of maternal psychosocial and clinical conditions during gestation and puerperal period on preschool children's behavior.

Methods:
A longitudinal quantitative cohort study was conducted, with a convenience sample of 103 women with preschool children (aged 3 to 5 years) residing in Porto Alegre, Brazil. Participants were recruited 48 hours postpartum and followed for the first six months of the child's life and throughout preschool years. Sociodemographic and clinical questionnaires were administered, and child behavior was assessed using the Strengths and Difficulties Questionnaire (SDQ). The main maternal clinical and psychosocial factors during the gestational and postpartum periods were correlated with the SDQ factors and total score using Pearson coefficient, and those that were statistically significant underwent multiple linear regression analysis. All ethical aspects of research with human beings were respected (Ethics Committee #11-0097 and #11-027).

Results:
Findings revealed that the mother’s education level and the number of people in the household were associated with increased behavioral difficulties in children. Psychosocial factors such as unplanned pregnancies, postpartum depressive symptoms, and weak maternal bonding three months after childbirth explained elevated levels of behavioral issues. Specifically, depressive symptoms and weak bonding were linked to emotional difficulties, while unplanned pregnancies were associated with hyperactivity. Experiences of physical aggression during pregnancy also were associated with behavioral problems in children. No significant associations were found for gestational clinical conditions.

Conclusions:
Maternal psychosocial conditions can significantly impact preschool children's behavior. These findings highlight the importance of interventions focused on maternal mental health to promote healthy child development.

Funding:
Coordination for the Improvement of Higher Education Personnel (CAPES) and National Council for Scientific and Technological Development (CNPq).

Key-words: (up to 5):

Psychossocial factors; gestational clinical conditions; child behavior; child development; pre-school age.

Abstract #00005701 en

Social Factors and Sugary Drinks as Predictors for Dental Caries, Periodontitis, and Hypertension in Pregnant Women: A Machine Learning Approach

Big Data and Cohorts in DOHaD Research.

Ribeiro Cecilia Claudia Costa (1), Sá Rafaela Vitoria Pereira (2), Viola Poliana Cristina Fonseca (2), Thomaz Erika Barbara Fonseca (2), Sousa Bruno Feres (2)
(1) Federal University of Maranhão, (2) Federal University of Maranhão (UFMA)

Background/aims:
Dental caries, periodontitis, and hypertension are major noncommunicable diseases affecting pregnant women. These conditions are interrelated and have been associated with adverse birth outcomes, such as preterm birth and low birth weight. This study aimed to analyze socioeconomic and behavioral prenatal indicators using machine learning algorithms to predict the occurrence of caries, periodontitis, and hypertension in pregnant women.

Methods:
This study used data from the BRISA prenatal cohort in São Luís, Brazil, including a sample of pregnant women (n = 1,447). Calibrated dentists assessed dental caries (using the DMFT index) and periodontitis. Based on medical diagnosis, gestational hypertension was identified. Machine learning techniques were applied to test a set of predictors, and the contribution of each variable to the models was evaluated using the Shapley Additive exPlanations (SHAP) method.

Results:
The prevalence rates of dental caries, periodontitis, and hypertension were 68%, 40.6%, and 18.3%, respectively. Model accuracies ranged from 50% for periodontitis to 63% for hypertension. Sensitivities were 55% for caries, 47.7% for periodontitis, and 50.5% for hypertension, while specificities were 58%, 51.8%, and 66.7%, respectively. SHAP analysis identified social factors—low family income, fewer years of schooling, and soft drink consumption—as the main common predictors across all outcomes. Pregestational overweight and advanced maternal age were also among the top five predictors for hypertension.

Conclusions:
Our findings underscore the influence of social determinants and sugary drink consumption on noncommunicable diseases during pregnancy. Strategies to reduce socioeconomic inequalities and promote healthier behaviors during pregnancy may be key to improving maternal health and preventing adverse birth outcomes.

Funding:
This work was supported by the Brazilian Ministry of Health/DECIT/CNPq in partnership with the Gates Foundation [no. 400759/2024-1].

Key-words: (up to 5):
caries, periodontitis, hypertension, pregnant women, machine learning algorithms

Abstract #00005702 en

Factors influencing growth at 12 month-corrected age in Chinese very preterm infants: A prospective cohort study

Impact of Early Life Exposures and Environmental Pollutants

Olga Laurentya (1), Zhao Li-Jin (2), Zheng Wen-Ting (2), Cao Jie (2), Wang Ke (2), Liu Jin-Feng (2), Duan Xia (2) (1) West Suffolk Hospital, (2) Shanghai First Maternity and Infant Hospital

Background/aims:
Very preterm infants (VPI) face significant challenges in achieving optimal growth, yet data on Chinese VPI are limited. According to the Developmental Origins of Health and Disease (DOHaD) theory, early growth is crucial for long-term metabolic health, particularly among those exposed to intrauterine insults such as prematurity. This study aimed to investigate factors affecting growth among Chinese VPI during the first year of life.

Methods:
We conducted a prospective cohort study of 223 VPI (28–32 weeks' gestation) in Shanghai, China (2020–2022). Growth parameters, including weight, length, and head circumference, were measured between 1 and 12 months of age. Multiple linear and logistic regression analyses were used to identify factors associated with growth outcomes, including maternal physical and mental health and immediate birth outcomes (as reflected by APGAR scores).

Results:
Maternal postpartum depression was associated with reduced weight (B = -0.02, p = 0.025), length (B = -0.16, p = 0.016), and head circumference (B = -0.03, p = 0.435). Preeclampsia (length: B = -0.28, p = 0.007) and subclinical hypothyroidism (head circumference: B = -2.58, p = 0.006) were also linked to poorer growth outcomes. Infant factors associated with reduced growth included lower birth weight (weight: B = 0.00, p = 0.001), male sex (length: B = -0.79, p < 0.001), and congenital heart disease (weight: B = -0.23, p = 0.090). In contrast, higher 1-minute Apgar scores (length: B = 0.02, p = 0.037) and exclusive breastfeeding (length: B = -0.36, p = 0.007) were positively associated with growth.

Conclusions:
Maternal factors, including postpartum depression, preeclampsia, and subclinical hypothyroidism, alongside infant characteristics such as birth weight and sex, significantly influenced growth among Chinese VPI. These findings highlight the importance of targeted early interventions to optimise growth in this high-risk group.

Funding:
National Natural Science Foundation of China Youth Project and Shanghai Nursing Society outstanding young talents seedling programme

Key-words: (up to 5):
Very preterm infant, infancy growth, maternal depression, maternal morbidities, DOHaD

Abstract #00005705 en

Hepatic characterization of physiopatological alterations in a mouse model of maternal hipercolesterolemia and the effects of a polyphenol-enriched-extra-virgin-olive-oil (EVOO) nutritional intervention

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Riquelme Marchant Nicolás Andrés (1), Rios Vanessa (1), Morales Andrea (1), Saavedra Fujiko (2), Illanes Sebastián (2), Busso Dolores (2), Yañez Maria (1), Leiva Andrea (1) (1) Universidad San Sebastian, (2) Universidad de los Andes

Background/aims:
Maternal supraphysiological hypercholesterolemia (MSPH) affects approximately 20-30% of human pregnancies and is associated with increased maternal oxidative stress, endothelial dysfunction, pro-atherogenic lipoproteins, and higher cardiovascular risk.
The liver is particularly susceptible to metabolic overload, such as that induced by hypercholesterolemia. Hepatic mitochondria, crucial for cellular energy production, are especially vulnerable to these metabolic disturbances. Therefore, the use of animal models is critical for understanding of the hepatic consequences of MSPH.
Extra-virgin-olive-oil (EVOO), rich in antioxidant polyphenols, represents an interesting nutritional intervention for cardiovascular health and potentially beneficial for women with MSPH. This study aims to characterize the hepatic pathophysiological changes associated with steatosis and explore potential mitochondrial alterations induced by an atherogenic diet (ATR).

Methods:
Pregnant C57BL/6 mice were randomly distributed to diet control (chow), ATR (2% cholesterol + 0,5% sodium cholate) or EVOO (2% cholesterol + 0,5% sodium cholate + 12% EVOO) from gestational day (GD) 12.5 to 17.5). Maternal serum lipids, hepatic oxidative stress (Dihydroethidium, DHE), histology (Hematoxilin/eosin, H&E) and expression of genes related to lipid metabolism inflammation, and mitochondrial dynamics were analyzed. Statistical analyses were performed using Kruskal-Wallis test.
Approved by ethical scientific committee of Universidad de los Andes CEC2023035.

Results:
In maternal serum and liver, total cholesterol (TC) levels were elevated in ATR, an effect reversed by EVOO. In maternal serum, triglyceride (TG) levels decreased with both ATR and EVOO. In contrast, in liver tissue, TG levels and lipid droplet accumulation increased in both ATR and EVOO compared to control. There was a trend toward increased IL-6 levels and decreased PGC1α expression in ATR and EVOO. Additionally, LDL receptor levels were reduced in ATR and EVOO compared to control. Hepatic oxidative stress was elevated in ATR, an effect that was reversed by EVOO.

Conclusions:
ATR is associated with hepatic steatosis and oxidative stress, and elevated TC levels.

Funding:
FONDECYT 1230527-11200592-1251012.

Key-words: (up to 5):

Hypercholesterolemia, lipid metabolism, liver, mitochondria, extra-virgin-olive-oil.

Abstract #00005706 en

Climate Change as a Developmental Origin of Health and Disease: Investigating Prenatal and Early-Life Environmental Exposures on Intergenerational Health Trajectories

Effects of Environmental Climate Change on Early Life Health Setting in Future Generations.

Cândido dos Santos Neto Joaquim (1), Marcio Teodoro Cordeiro Silva Antonio (2)
(1) Faculty of Medicine of the Federal University of Goiás, (2) Graduate Program in Environmental and Health Sciences, Pontifical Catholic University of Goiás

Background/aims:
Climate change exacerbates environmental threats such as air pollution and extreme heat, which disproportionately affect vulnerable populations, including pregnant women and children. Emerging evidence links prenatal and early-life exposure to climate-driven stressors (e.g., particulate matter [$PM_{2.5}$], heatwaves) with adverse maternal-fetal outcomes and long-term offspring health. This study synthesizes data on how climate change alters early-life health trajectories, focusing on placental dysfunction, epigenetic changes, and transgenerational disease risks.

Methods:
A systematic review was conducted using PubMed (2019–2023) with keywords: climate change AND (pregnancy OR fetal development OR child health). Included studies assessed maternal/fetal outcomes tied to temperature extremes, air pollution, or extreme weather. Data were stratified by exposure type (heat, $PM_{2.5}$, wildfires) and outcomes (preterm birth, neurodevelopment, cardiovascular health). Quality was assessed via GRADE criteria.

Results:
Heatwaves increased risks of gestational hypertension (OR 1.4, 95% CI 1.1–1.8) and preterm birth (OR 1.6, 95% CI 1.3–2.0). $PM_{2.5}$ exposure correlated with placental inflammation ($p < 0.01$). Prenatal heat exposure is associated with low birth weight (−42g per 1°C increase) and neurodevelopmental delays (RR 1.3, 95% CI 1.1–1.5). Wildfire smoke raised childhood asthma incidence by 23%. Epigenetic modifications (e.g., DNA methylation) and oxidative stress were implicated in transgenerational effects.

Conclusions:
Climate change acts as a developmental disruptor, amplifying lifelong and intergenerational health disparities. Policy interventions must integrate DOHaD principles to mitigate risks, particularly in low-resource settings.

Funding:
No external funding was received.

Key-words: (up to 5):
Climate-vulnerable regions, longitudinal cohorts, Environmental Exposures, Prenatal.

Abstract #00005711 en

Maternal Malnutrition Induces Inflammatory Pathways and Oxidative Stress in the Dorsolateral Prostate of Male Offspring Rats

Mechanisms Determining Transgenerational Effects of Health and Disease

Mattos Renato (1), Naia Fioretto Matheus (1), Frediani Portela Luiz Marcos (1), Justulin Luis (1) (1) Sao Paulo State University (UNESP)

Background/aims:
Maternal conditions during pregnancy can influence the long-term health of offspring. In particular, maternal malnutrition (MM), such as protein restriction, affects the development of several organs, including the male reproductive system. This study examined how a low-protein maternal diet impacts the structure and function of the dorsolateral prostate (DLP) in aging male rats.

Methods:
Male offspring were divided into two groups: a control group (CTR), whose mothers received a normal protein diet (17%) during pregnancy and lactation, and a low-protein group (GLLP), whose mothers received a low-protein diet (6%) during the same period. At 540 days of age, the offspring were euthanized, and the DLPs were collected for analysis.

Results:
The GLLP group showed significant structural changes in the DLP, including increased epithelial and reduced stromal compartments. These rats also had lower levels of probasin (a prostate-specific protein), along with a higher number of mast cells, CD68+ macrophages, and IL-10 protein expression, indicating inflammation. Antioxidant balance was disrupted: glutathione (GSH) levels increased, while catalase (CAT) and superoxide dismutase (SOD) decreased. The expression of SIRT1, a protein linked to aging and oxidative stress control, was reduced. In silico analysis using human prostate cancer data (PRAD-TCGA) revealed that biological pathways related to oxidative stress, immune response, and tissue remodeling were disrupted in both the rat model and human prostate cancer.

Conclusions:
In summary, maternal protein restriction leads to long-term changes in the prostate of aging male offspring, including inflammation, oxidative stress, and tissue remodeling. The reduced expression of SIRT1 may play a key role in these effects.

Funding:
São Paulo Reseach Foundation (FAPESP). Grant number 2023/01714-9; 2022/03990-0
Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). Grant number 310663/2018-0.

Key-words: (up to 5):
Maternal malnutrition, dorsolateral prostate, oxidative stress, inflammation

Abstract #00005714 en

Does Maternal Malnutrition Alter Transposable Element Expression in the Rat Prostate and Contribute to the Developmental Origin of Prostate Cancer?

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Portela Luiz Marcos Frediani (1), Nascimento Oliveira Jordana Inacio (2), Ferreira Marcel Rodrigues (3), Mattos Renato (1), Bravo Isabella Lopes (1), Lorente Ana Beathriz Leite (1), Ribeiro Marcelo Augusto (1), Baptista Hecttor Sebastian (1), Justulin Luis Antonio (1)

(1) Institute of Biosciences, São Paulo State University, Brazil, (2) Faculty of Sciences, University of Ottawa- Canada , (3) Botucatu Medical School, São Paulo State University, Brazil

Background/aims:

The DOHaD concept establishes the association between disease throughout the lifespan and the early stages of development. Exposure of dam rats to maternal malnutrition is associated with impairment in prostate growth during early-life and an increase in prostate cancer (PCa) incidence during ageing. Here, we use RNA-Seq data to identify transposable elements (TEs) expressed in the prostate and their role of enhancer of gene expression in the prostate during early life and aging to the developmental origin of PCa.

Methods:

We performed RNA-Seq of the ventral prostate of control (CTR, offspring of mothers fed 17% protein) and malnourished (GLLP, offspring of mothers fed 6% protein) animals on postnatal day (PND) 21 and 540 (n=4 animals per group/age/technique). We develop repetitive elements annotation in genome Rattus norvegicus (mRatBN7.2) using RepeatMasker tool and aligned the reads using STAR. Reads were quantified using TEtranscripts, differential expression (DE) analysis of TEs was performed with DESeq2 $|Log2\ FC| \geq 1.0$ and an p-value < 0.05. Functional enrichment analyses were performed with gprofiler.

Results:

Genome analysis revealed TEs with the highest number of copies and predominantly LINEs, LTRs, and SINEs were identified. At PND21, we identified 18 DE TEs (13 down and 6 upregulated). At PND540, 13 TEs (11 down and 2 upregulated), with three commonly deregulated in both ages were identified. These TEs had 18,740 copies in the genome. Looking at the role of TEs as enhancers, we identified genes that were 2 kbp upstream of TEs and were DE in the prostate in GLLP group. In PDN21, 70 neighbours' genes regulate differentiation and anatomical development process, in PND540 12 genes were identified regulating cellular senescence pathways, energy metabolism, and IL-23.

Conclusions:

Our results suggest that TEs may act as enhancers of important genes for prostate homeostasis, which may act as precursors of the developmental origin of PCa.

Funding:

FAPESP 2021/00340-2 and 2022/03990-0.

Key-words: (up to 5):

DOHaD, transposable elements, development, inflammation, prostate cancer.

Abstract #00005716 en

Maternal protein restriction programs oxidative stress and secretory dysfunction in male offspring pancreas

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Leite Lorente Ana Beathriz (1), Pesse Vanessa Bonassa (1), Portela Luiz Marcos Frediani (1), Barata Luisa Annibal (1), Mattos Renato (1), Fioretto Matheus Naia (1), Baptista Hecttor Sebastian (1), Souza Franciane Quintanilha Gallego (2), Santos Débora Cristina Damasceno Meireles (2), Lima Clélia Akiko Hiruma (1), Fagundes Felipe Leonardo (1),
Justulin Luis Antonio (1)
(1) São Paulo State University / Institute of Biosciences of Botucatu, (2) São Paulo State University / Botucatu Medical School

Background/aims:
Maternal protein restriction (MPR) is known to induce metabolic reprogramming in offspring, leading to adult-onset metabolic syndromes like type 2 diabetes mellitus. However, pancreatic alterations in these offspring remain unclear. Therefore, this study aimed to assess the pancreatic morphophysiology and oxidative status of animals subjected to MPR.

Methods:
For this purpose, male Sprague Dawley rats were divided into groups CTR (control, offspring of mothers fed a 17% protein diet during pregnancy and lactation) and GLLP (restricted, offspring of mothers fed a 6% protein diet during pregnancy and lactation) (CEUA5119280121). The animals were weighed and euthanized on postnatal day (PND) 21 for blood and pancreas collection. Pancreatic samples were processed for morphological analysis (n=6), colorimetric assays to measure activity of SOD, CAT and GSH (n=6), and protein expression analysis for insulin, glucagon, somatostatin and the antioxidant enzymes of the PRDX 1-4 family (n=6). Serum insulin levels were also measured.

Results:
GLLP animals showed reduced body weight (47.56 ± 9.86 vs. 20.56 ± 3.99), pancreatic weight (absolute: 188.8 ± 47.14 vs. 49.48 ± 7.69; relative: 4.33 ± 0.95 vs. 2.51 ± 0.41), and serum insulin levels (1.73 ± 0.98 vs. 0.26 ± 0.13). In addition, we observed a reduction in blood glucose levels, a decrease in insulin secretion, and an increase in glucagon secretion in the GLLP group, along with a lower frequency of larger pancreatic islets. Regarding pancreatic oxidative status, we found a reduction in the enzymatic activity of SOD (1.16 ± 0.3 vs. 0.89 ± 0.09) and CAT (9.303 ± 5.165 vs. 3.225 ± 2.235), along with an increased expression of PRDX2 and decreased expression of PRDX3 and PRDX4.

Conclusions:
Our findings demonstrate that MPR induces delayed development and structural, metabolic, and functional changes in the pancreatic gland, thereby increasing the risk of developing pancreatic pathologies throughout life.

Funding:
FAPESP 2023/06412-0.

Key-words: (up to 5):
Maternal malnutrition DOHaD Pancreas Islets Rats

Abstract #00005727 en

Role of placental leptin secretion and PCSK9 expression in the genesis of maternal supraphysiological hypercholesterolemia

Mechanisms Determining Transgenerational Effects of Health and Disease

Morales Garrido Andrea (1), Illanes Sebastián (2), Kerr Bredford (3), Leiva Andrea (4), Yañez María José (4)
(1) Universidad San Sebastian , (2) Facultad de Medicina, Universidad de Los Andes., (3) Centro de Biología Celular y Biomedicina, Facultad de Ciencias, Universidad San Sebastián, (4) Facultad de Ciencias, Universidad San Sebastián

Background/aims:
During pregnancy, maternal total cholesterol (TC) levels physiologically increase to support fetal development. However, in approximately 30% of pregnancies, this increase is excessive (TC≥280mg/dL), resulting in maternal supraphysiological hypercholesterolemia (MSPH). Although its cause is not fully understood, elevated PCSK9 levels have been identified as a key regulator, as PCSK9 promotes the degradation of the hepatic LDL receptor (LDLR), thereby increasing circulating LDL levels. Since the placenta secretes leptin, it has been suggested that this leptin may contribute to the dyslipidemia observed in MSPH. dyslipidemia.
Aim: To assess placental leptin secretion, PCSK9 expression, and their association with maternal lipid profile.

Methods:
Placentas were collected at delivery from women with MPH (TC < 280 mg/dL, n=6) and MSPH (TC ≥ 280 mg/dL, n=7). Maternal serum LDL, TC, and leptin were measured by enzymatic assay and ELISA. Placental PCSK9 expression was assessed by qPCR and Western blot. Explants were cultured for 6 and 20 hours, and leptin levels in conditioned media (CM) were measured. Mann-Whitney and Spearman correlation tests were applied. Ethical approval: CEC2022023.

Results:
At delivery, MSPH mothers had twofold higher serum leptin levels and increased placental leptin mRNA expression compared to MPH ($p < 0.001$). Placental PCSK9 protein levels were also elevated ($p < 0.001$). CM from MSPH placentas showed higher leptin levels, with a near threefold increase after 20h incubation ($p < 0.01$). Maternal leptin levels correlated positively with LDL ($r=0.64$; $p= 0.0221$), but not TC ($r= 0.46$; $p= 0.1131$).

Conclusions:
MSPH is associated with increased placental leptin secretion and PCSK9 expression, suggesting a role for leptin in maternal lipid dysregulation during pregnancy.

Funding:
FONDECYT 11200592 and 1251012

Key-words: (up to 5):
Leptin, PCSK9, Maternal Supraphysiological Hypercholesterolemia, Placenta, Lipid Metabolism.

Abstract #00005728 en

The relationship between maternal and umbilical cord 25(OH)D concentrations: The Araraquara Cohort Study

Public Health Policies Across the Life Cycle.

Oliveira Aires Isabel (1), Alves Luzia Liania (1), Ramos Silva Tamiris (1), Pinheiro-Castro Natália (1), Pereira Lopes Aldaisa (1), da Silva Lima Eloise (1), Antonia Martins Rodrigues Francilany (1), Victor Audencio (1), Helen de Carvalho Rondó Patrícia (1)
(1) School of Public Health, University of São Paulo

Background/aims:
Vitamin D [25(OH)D] is essential for fetal development because it is transferred from the mother to the fetus across the placenta. Previous studies have shown that the concentration of 25(OH)D in cord blood mainly reflects maternal levels, but few studies have evaluated this relationship longitudinally during pregnancy. The aim of this study was to investigate the relationship between maternal 25(OH)D concentrations at different gestational ages and 25(OH)D levels in cord blood.

Methods:
Prospective longitudinal study of 156 mother-child pairs participating in the Araraquara Cohort Study, conducted in the city of Araraquara, SP, Brazil [Ethics Committee: 67483517.6.0000.5421]. Serum 25(OH)D concentrations were measured by chemiluminescence at three periods (<19, 20-28, and 30-38 weeks) and in cord blood. Linear regression analyses were performed to assess the relationship between maternal and cord blood 25(OH)D concentrations, adjusted for gestational age. The statistical significance adopted was $p<0.05$.

Results:
The median 25(OH)D concentrations of the participants were: 62.5 (50-75) nmol/L in 1st period, 65 (55-77.5) nmol/L in 2nd period, and 70 (55-82.5) nmol/L in 3rd period. The median in cord blood was 80 (67.5-95) nmol/L. A significant association was observed between maternal and cord blood 25(OH)D concentrations in all periods investigated, with a progressive increase in the strength of the association throughout pregnancy – 1st period: $R^2 = 0.028$; $p = 0.038$; 2nd period: $R^2 = 0.17$; $p < 0.001$ and 3rd period: $R^2 = 0.27$; $p < 0.001$.

Conclusions:
The results show an increasing positive association between maternal and fetal 25(OH)D concentrations throughout pregnancy, with the greatest explanation of variability in the period between 30 and 38 weeks of gestation. This reinforces the importance of maternal status of this nutrient at the end of pregnancy as the main determinant of fetal levels at birth.

Funding:
Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) – grant numbers: 2015/03333-6 and 2024/01014-0.

Key-words: (up to 5):
vitamin D, pregnancy, cord blood, cohort study.

Abstract #00005729 en

Maternal obesity negatively programs offspring hepatic lipidomics and transcriptomics predisposing to premature aging and fatty liver in a sex-dependent manner

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Lomas-Soria C (1), Nathanielsz PW (2), Zambrano E (3)
(1) Biología de la Reproducción INCMNSZ/ Centro de Investigación sobre Envejecimiento(CIE-CINVESTAV Sur), (2) Wyoming Center for Pregnancy and Life Course Health Research, Department of Animal Science, (3) Biol Reproducción, Instituto Nacional de Ciencias Médicas y Nutrición SZ/Facultad de Química UNAM

Background/aims:
Several studies showed that programming of rat offspring by maternal obesity accelerates the development of metabolic dysfunction and premature aging. Altered lipid metabolism and signaling is implicated in aging yet no studies address lipid programming-aging interactions. C16:0 ceramides (CER) plays a key role in development of insulin resistance, a characteristic of both NAFLD and aging. We aimed to evaluate offspring liver mechanisms responsible for the predisposition to early fatty liver with lipidomic and transcriptomic approaches in C and MO offspring.

Methods:
F0 female rats ate control (C) or obesogenic diet (MO) from weaning through pregnancy and lactation. After weaning all offspring (F1) ate C diet so later life differences are due to maternal dietary programming of F1. Offspring ages were young adult (110 d) and mature adult (650 d), providing four experimental groups C110, MO110, C650 and MO650 for each sex. We determined F1 liver lipidome by mass spectrometry and transcriptome (RNA-seq). M±SEM, Two-way ANOVA, Tukey test α=0.05.

Results:
CER C16:0 in liver increases with age in C and MO, while CER species containing longer fatty acid chains (e.g., C24:0) were reduced in male offspring. Whereas F1 Female values of C16:0 and C24:0 CER showed no change in all groups. Total lysophosphatidylcholines (LPC), triacylglycerol and fatty acids in liver were increased in MO650 vs C650 in males, but no changes in female groups. Sphingolipid signaling and metabolic KEGG pathways were upregulated in F1 males and down regulated in F1 females in MO650 vs C650.

Conclusions:
Ceramides and sphingolipids increase insulin resistance and down-regulate genes involved in fatty acid oxidation, leading to hepatic steatosis. Maternal obesity adversely programs offspring liver lipid signaling and metabolic dysfunction, which affects the natural trajectory of metabolic aging, potentially predisposing offspring to the development of fatty liver early in life in a sex-dependent manner.

Funding:
Newton Fund RCUK-CONACyT FONCICYT/49/2016

Key-words: (up to 5):
Obese mothers, NAFLD, lipid metabolism, aging

Abstract #00005731 en

Assessment of a Personalized mHealth App on Micronutrient Supplement Use in Pregnancy in Karachi, Pakistan

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Nuruddin Rozina (1), Vadsaria Khadija (1), Mohammed Nuruddin (2), Azam Iqbal (1), Sayani Saleem (3) (1) Aga Khan University, (2) Aga Khan University Hospital, (3) Aga Khan Development Network

Background/aims:
Micronutrient deficiencies during pregnancy are widespread in developing countries and pose serious risks to maternal and newborn health. Folic acid, iron, calcium and vitamin D supplementation is critical, yet adherence remains a major challenge. This study investigated the effectiveness of a personalized mobile health (mHealth) intervention in promoting consistent supplement use among pregnant women.

Methods:
A randomized controlled trial was conducted at Aga Khan University Hospital (January 2020 and September 2021), enrolling 306 first-trimester pregnant women with smartphones. The intervention group received personalized micronutrient supplement coaching through an mHealth app (PurUmeed Aaghaz) as thrice-weekly push messages and tailored recommendations over 24 weeks. The comparison group received standard face-to-face counselling at 6, 12, 18, and 24 weeks after enrollment. Weekly supplement use was scored 0 (daily), 1.5 (4-6 times weekly), and 3 (≤3 times weekly), with a cumulative supplement use score (CSUS) ranging from 0-12 across 4 supplements. Every fourth woman underwent biochemical micronutrient assessment. Data were analyzed using Stata v.14, with random-effects panel regression.

Results:
107 (69.9%) intervention-group participants and 125 (81.7%) non-intervention-group participants completed the study. After 24 weeks, the intervention group showed a greater but insignificant reduction in mean CSUS (β:–0.27, 95% CI:−0.65 to 0.12). Daily supplement use improved for folic acid (20% vs. 22.4%), iron (11.2 vs. 2.1 times), calcium (1.2 vs.14.2 times), and vitamin D (3 vs.1.3 times). Multivariable analysis showed higher but insignificant odds of sufficient folic acid (aOR:1.26, 95% CI:0.68-2.36) and iron use (aOR:1.31, 95% CI:0.95-1.81) whereas vitamin D use was significantly higher (aOR:1.88, 95% CI:1.43-2.47) in the intervention group and calcium intake improved in the nonintervention group (aOR:0.59, 95% CI:0.44-0.79). Anaemia decreased in the intervention group, but other deficiencies persisted in both groups.

Conclusions:
An affordable, accessible, and personalized mHealth intervention has the potential to enhance antenatal supplementation, particularly vitamin D use during pregnancy.

Funding:
Funding for this study was received from the University Research Council of Aga Khan University. Funds for biochemical assessment were received from the Faculty of Health Sciences PhD program of Aga Khan
University

Key-words: (up to 5):

micronutrients, mobile health, Pakistan, pregnancy, supplements

Abstract #00005733 en

Diet-induced obesity decreases circulating endocannabinoids in pregnant rats and differentially regulates male and female placental cannabinoid receptor expression

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Santos Lucas (1), Alaburda Letícia (1), Calvino Camila (1), Muller Verônica (1), Gomes Clara (1), Pena Juliana (1), Pazos-Moura Carmen (1), Andrade Cherley (2), Trevenzoli Isis (1)
(1) Universidade Federal do Rio de Janeiro, (2) Universidade do Estado do Rio de Janeiro

Background/aims:
Maternal obesity is associated with placental dysfunction and overactivation of the offspring's endocannabinoid system (ECS). The ECS is a lipid signaling system that induces lipogenesis, inflammation and hyperphagia. We evaluate the effect of diet-induced obesity on maternal circulating endocannabinoids and placental cannabinoid receptors (CB1 and CB2) in rats.

Methods:
Female rats were fed a control diet (C; 10% lipids) or an obesogenic diet (OD; 39% lipids, 9.5% sucrose) for 9 weeks before and during pregnancy (Ethics protocol n° 147/21). On the 20th gestational day, cesarean section was performed to collect placentas and fetuses. Maternal, placental and fetal anthropometric and metabolic parameters were recorded. Endocannabinoids were evaluated by mass spectrometry, and placental CB1 and CB2 by immunohistochemistry. Data were analyzed by Student's t-test and Two-way ANOVA ($p<0.05$*).

Results:
Diet-induced obesity increased body weight (+8.7%*), glucose intolerance (+15%*) and visceral adiposity (+50.2%*), while decreased serum levels of the endocannabinoid 2-arachidonoylglycerol (2-AG) (-58%*) in OD rats. OD increased placental triglycerides and the fetal/placental weight ratio ($p<0.05$). OD decreased CB1 in the junctional zone (Jz) (-69%*) and increased in the labyrinth zone (Lz) (+43%*) in male placentas, with no changes in female. OD decreased CB2 in the Jz regardless of fetal sex ($p=0.0012$).

Conclusions:
Diet-induced obesity decreased maternal 2-AG levels, which may have a potential deleterious impact on fetal neurodevelopment. OD increased placental triglycerides, and lipotoxicity has been associated with placental dysfunction and negative metabolic outcomes in offspring. An increased fetal/placental weight ratio suggests an adaptive response aimed at preserving fetal growth. Increased Lz CB1 expression may be part of this adaptation, as it stimulates the expression of placental growth factors. However, CB1 induces lipogenesis and oxidative stress. Additionally, decreased Jz CB2 may be associated with a proinflammatory environment, potentially affecting on placental hormone production.

Funding:
CAPES,FAPERJ,CNPQ

Key-words: (up to 5):
Maternal obesity. Endocannabinoid system. Placenta.

Abstract #00005734 en

Maternal obesity increases endocannabinoid signaling and triglyceride content in the liver of rat offspring at weaning

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Fassarella Larissa (1), Dias Thamiris (1), Calviño Camila (1), Gonçalves Juliana (1), Torres Alexandre (1), El Bacha Tatiana (1), Ferreira Carolina (1), Pazos-Moura Carmen (1), Trevenzoli Isis (1)
(1) Universidade Federal do Rio de Janeiro

Background/aims:
Maternal obesity may predispose offspring to metabolic dysfunction-associated steatotic liver disease (MASLD), which is related to endocannabinoid system (ECS) overactivity. The ECS comprises the endocannabinoids anandamide and 2-arachidonoylglycerol (2-AG), cannabinoid receptors, and several metabolizing enzymes, as the monoacylglycerol lipase (MAGL). We hypothesized that maternal obesity would promote liver steatosis in weanling rat offspring associated with increased endocannabinoids and modulation of their metabolizing enzymes.

Methods:
Female rats (60 days old) were fed a control diet (CT; 9% kcal lipids) or an obesogenic diet (OD; 40% kcal lipids +9.5% kcal sucrose) for 9 weeks before mating and during gestation and lactation (Ethics protocol n. 059/19). Offspring liver was collected at weaning for analysis of endocannabinoids (high performance liquid chromatography/ mass spectrometry), fatty acids (gas chromatography/flame ionization detection) and ECS enzymes (Western Blotting). Data were analyzed by two-way ANOVA and Pearson correlation tests, with significance at $p<0.05$.

Results:
Maternal obesity increased the content of triglycerides, 2-AG, and saturated, monounsaturated and polyunsaturated fatty acids (PUFA) in the offspring liver ($p<0.05$), regardless of sex. Maternal obesity reduced n-3 PUFA content while increased n-6 PUFA in both sexes ($p<0.05$), elevating the n-6/n-3 ratio at weaning ($p<0.05$). Increased 2-AG was associated with reduced MAGL expression in both sexes ($p<0.05$). Hepatic 2-AG showed a negative correlation with n-3 PUFA (males: $r= -0.5435$; $p<0.05$; females: $r= -0.6494$; $p>0.05$) and a positive correlation with the n-6/n-3 ratio (males: $r= 0.6288$; $p<0.05$ 0.0091; females: $r= 0.8565$; $p<0.05$), regardless of offspring sex.

Conclusions:
Maternal obesity induced early hepatic steatosis and reduced MAGL expression, possibly causing the increase of liver 2-AG. Increased ECS signaling in the liver can result in lipogenesis, oxidative stress and inflammation. These findings suggest that maternal obesity can increase the risk of MASLD associated with ECS modulation.

Funding:
FAPERJ, CNPq, CAPES.

Key-words: (up to 5):
Endocannabinoid system. Maternal obesity. Liver steatosis.

Abstract #00005735 en

Modelling gestational weight gain trajectories using SITAR models: Findings from two Brazilian cohort studies

Big Data and Cohorts in DOHaD Research.

Victor Audêncio (1), Silva Tamiris (1), Lopes Aldaisa (1), Penzias Rebecca (2), Luzia Liania (1), Rondó Patricia (3), Ohuma Eric (2)

(1) University of São Paulo, School of Public Health, São Paulo, SP, Brazil, (2) London School of Hygiene and Tropical Medicine, London, UK, (3) University of São Paulo, School of Public Health

Background/aims:

Gestational weight gain (GWG) is a key maternal and neonatal health outcome determinant. Understanding the trajectory of GWG, beyond its total amount, offers valuable insights for early risk identification and targeted interventions. This study aimed to apply the SITAR (Super Imposition by Translation and Rotation) growth model to individual GWG trajectories in two Brazilian cohorts.

Methods:

We analysed longitudinal data from 3,770 pregnant women enrolled in two population-based cohorts in São Paulo state, Brazil (Araraquara: n=2,805; Jundiaí: n=965). Maternal weight was recorded at each trimester. GWG was modelled using the SITAR nonlinear mixed-effects model. Model performance was assessed by Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and percentage of variance explained.

Results:

The SITAR models converged satisfactorily after simplification, explaining 84.0% and 85.6% of the variance in GWG trajectories in Araraquara and Jundiaí, respectively. In Araraquara, the peak velocity of weight gain occurred at 24.5 weeks with a maximum rate of 0.37 kg/week; in Jundiaí, the peak occurred at 28.2 weeks with a rate of 0.41 kg/week. Fixed effect estimates for size and acceleration were negative in both cohorts, suggesting a general downward shift in weight gain trajectories relative to the cohort means.

Conclusions:

The SITAR model, after appropriate simplifications, provided a robust and biologically meaningful description of GWG trajectories in Brazilian pregnant women. Incorporating SITAR-based parameters into maternal health surveillance could enhance early identification of atypical weight gain patterns and inform more personalized prenatal care strategies, supporting public health efforts to improve maternal and neonatal outcomes.

Funding:

São Paulo State Foundation-FAPESP (grants: 1998/0321-0; 2015/03333-6). AV and TS received scholarships from FAPESP (grant number 2023/07936-3; 2024/18309-2; 2023/02404-3).

Key-words: (up to 5):

Gestational weight gain; SITAR model; growth trajectories; maternal health; epidemiology.

Abstract #00005737 en

Can personalized counselling through Mobile Health Application influence Maternal and Newborn Outcomes? A Randomized Controlled Trial

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Vadsaria Khadija (1), Nuruddin Rozina (1), Mohammed Nuruddin (1), Sayani Saleem (2), Azam Iqbal (1) (1) Aga Khan University, (2) Aga Khan Development Network

Background/aims:
Digital health tools offer a promising avenue for delivering tailored counselling to pregnant women addressing critical behaviours like dietary modification, supplement use, and physical activity. Despite their growing relevance, their application during pregnancy remains understudied in Pakistan. This study evaluated the effectiveness of a mobile health (mHealth) intervention on maternal and newborn outcomes compared to standard counselling.

Methods:
In a randomized controlled trial at Aga Khan University, 306 pregnant women enrolled at the first trimester were assigned to either an intervention or control group. The former group received 24 weeks of counselling via the locally developed PurUmeed Aaghaz app focusing on dietary habits, micronutrient supplementation, and physical activity. The latter group received standard face-to-face counselling at 6, 12, 18, and 24 weeks post-enrollment. Maternal outcomes included incidence of gestational hypertension, preeclampsia and gestational diabetes mellitus (GDM) assessed from medical records. Gestational weight gain (GWG) was calculated as the average weekly weight change between the first and third trimesters. Newborn outcomes included birth weight, length, and gestational age at delivery (GAD) compared using the INTERGROWTH-21st standards. Chi-square or Fisher's exact tests were performed in Stata 14.

Results:
Maternal and newborn outcomes data were available for n=110 and n=107 in the intervention group and n=128 and n=125 in the non-intervention group, respectively. Incidences of gestational hypertension (8.2% vs. 7%), preeclampsia (3.6% vs. 1.6%) and GDM (13.6% vs 23.4%) showed no statistically significant differences. Mean GWG and GAD were similar across groups. Preterm births occurred in 11.8% vs. 12.5% of cases. Mean birth weights (2.85 vs. 2.86 kg) and proportions of newborns ≤10th percentile for weight (14% vs. 12.8%) and length (2.9% vs. 0.8%) were also comparable.

Conclusions:
The mHealth intervention showed no significant impact on maternal or newborn outcomes. Further research with a larger sample size is needed to validate and build upon these findings

Funding:
Funding for this study was received from the University Research Council of Aga Khan University.

Key-words: (up to 5):
gestational diabetes mellitus, gestational hypertension, gestational weight gain, newborn outcomes, preeclampsia

Abstract #00005738 en

Breastfeeding Practices and Infant Feeding Perceptions in Women with Polycystic Ovary Syndrome Compared to Nutritional Status-Matched Controls

Role of Infant and Young Child Feeding Practices on Long-Term Health

Leiva Carla (1), Sánchez Francisca (2), Aguilera Gonzalo (1), Cárdenas Gabriela (3), Jorquera Pía (3), Valenzuela Rodrigo (2), Barrera Cynthia (2), Villablanca Claudia (2), Atencio Camila (2), Maliqueo Manuel (2)
(1) Universidad de Chile - Pontificia Universidad Católica de Chile , (2) Universidad de Chile, (3) Hospital Clínico San Borja Arriarán

Background/aims:
Polycystic ovary syndrome (PCOS) is a common endocrine disorder affecting women of reproductive age, associated with ovulatory dysfunction, metabolic alterations, and increased long-term cardiometabolic risk. Breastfeeding (BF) provides significant benefits for maternal and infant health. However, specific evidence regarding BF attitudes in women with PCOS remains limited. This study aimed to assess BF perceptions and metabolic health indicators among women with PCOS compared to eutrophic and overweight/obese controls.

Methods:
A descriptive cross-sectional study was conducted among 20 lactating women aged 18–36 years (mean BMI: 26.7 kg/m²), categorized into three groups: PCOS (n=4), eutrophic controls (BMI <25, n=5), and overweight/obese controls (BMI ≥25, n=11). Infant feeding attitudes were assessed using the Iowa Infant Feeding Attitude Scale (IOWA 2006). Clinical evaluations included anthropometric measurements and fasting biochemical profiles (total cholesterol, triglycerides, and glucose). Descriptive analyses and Kruskal-Wallis and chi-square tests were performed for group comparisons. All participants gave written consent (Ethics Committee #084-2024).

Results:
Seventy percent of participants practiced exclusive BF and had received prior lactation counseling. Seventy-five percent expressed favorable perceptions toward BF. The mean IOWA score was 53.9 points, suggesting an overall favorable attitude toward breastfeeding. The mean scores were 50.75 in the PCOS group, 52.2 in eutrophic controls, and 55.8 in overweight/obese controls, with no significant differences between groups (p=0.322). Mean biochemical parameters were within clinical reference ranges. A significant difference was observed regarding the perception that formula feeding is as healthy as breastfeeding (p=0.035), with higher agreement among women with PCOS.

Conclusions:
Although no significant differences in overall BF attitudes were detected between groups, observed trends suggest possible variations according to maternal condition and nutritional status. Possible factors influencing these perceptions include maternal age, socioeconomic status, available social support, and previous breastfeeding experience. Future studies should explore these contextual variables to better understand breastfeeding attitudes in women with and without PCOS.

Funding:
Proyecto SOCHINUT - Henry Nestlé 2023, Proyecto Sociedad Chilena de Endocrinología y Metabolismo (SOCHED) 2023, ANID Becas/Doctorado Nacional 21220507, Fondecyt regular 1241725.

Key-words: (up to 5):
Breastfeeding, Polycystic Ovary Syndrome, Metabolic Health, Infant Feeding Attitudes, Maternal Health.

Abstract #00005742 en

PLACENTAL EXPRESSION OF AMPK, DRP1, MFN1 AND DNMT1 IN GESTATIONAL DIABETES PATIENTS TREATED WITH METFORMIN

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Paulino Gonzalez Angel David (1), Pantoja Barroso Claudia Jimena (2), Villanueva Tapia Leydi Arlet (3), Barbosa Sabanero Gloria (2), Farchaud Roucher Veroniqué (4), Lazo De la Vega Monroy Maria Luisa (2) (1) University of Guanajuato , (2) Universidad de Guanajuato, (3) , (4) Nantes University

Background/aims:
Gestational diabetes mellitus (GD) is a highly prevalent complication of pregnancy. Metformin, a widely used drug for DG control, modulates mitochondrial activity. However, research regarding the effects of metformin on mitochondrial dynamics in the human placenta is limited. The aim of the present study was to assess if metformin treatment of GD modifies protein expression of mitochondrial dynamics in placenta of women with GD.

Methods:
We performed a cross-sectional study in placentas from healthy mothers (control) (n=20) or diagnosed with GD treated with metformin (GD-M) or with no pharmacological treatment (GD) (n=15 in each group), and their newborns.The study was approved by ethics committees (CIUBG-P49-2022/HEMIL CEI 20-2023).
AMPK expression and activation, MFN1, DRP1, and DNMT1 expression was evaluated by Western blot.
Data were analyzed by one-way ANOVA and Spearman´s correlation.

Results:
HbA1c and placental weight were higher in GD compared to control (p=0.008, p=0.006, respectively). GD-M newborns had lower birth weight than GD (p=0.0003). Birth length was higher in GD vs control
(p=.0009) and vs GD-M (p=0.002). Head circumference in GD was higher compared to the other groups (p=0.003).
VLDL (p=0.001) and triglycerides (p=0.01) were higher in GD-M vs control. pAMPK/AMPK ratio was lower in DG vs control (p=0.04). No differences in MFN1 and DRP1 expression were found, while DNMT1 was higher in GD-M vs control (p=0.04). pAMPK correlated gestational age (r=.33, p=0.01). pAMPK/ AMPK ratio correlated with maternal HbA1c (r=-.29, p=0.04), maternal cholesterol (r=-.27, p=0.04) and maternal LDL (r=-.31, p=0.02).
DRP1 correlated with MFN1 (r=.46, p=0.007), placental weight (r=.28, p=0.04), and umbilical cord glucose (r=.40, p=0.003).MFN1 correlated with maternal HbA1c (r=.29, p=0.03).

Conclusions:
GD decreases AMPK activation in placenta. Metformin restores AMPK activation and increases. DMNT1, an epigenetic modulator, without changes in mitochondrial dynamics proteins. Further studies are needed to elucidate other effects of metformin in the human placenta.

Funding:
This project was funded by University of Guanajuato UG-CIIC-105/2024 and UG-CIIC-2025.

Key-words: (up to 5):
Gestational diabetes, placenta, AMPK, mitochondria, metformin.

Abstract #00005743 en

Effects of a chili-supplemented diet on maternal obesity and non-alcoholic fatty liver disease programming

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Gutiérrez-Chávez Vanesa (1), Merino-Eugenio Karen (2), García-Morales Abigail (3), Pinzón Esmeralda (2), Reyes-Castro Luis A (2), Feregrino-Pérez Ana A (1), Guevara-González Ramón G (1), Lomas-Soria Consuelo (2)
(1) Ingeniería en Biosistemas, Facultad de Ingeniería, UAQ, Campus Amazcala, (2) Departamento de Biología de la Reproducción, INCMNSZ, (3) Doctorado en Ciencias Biológicas y de la Salud, UAM

Background/aims:
Maternal high-fat diet (HFD) is an important predisposing factor to the onset of metabolic diseases in offspring. The disability of fetuses to buffer excess transplacental lipids makes them susceptible to developing non-alcoholic fatty liver disease (NAFLD) at early stages of life. Capsinoids and capsaicinoids from chili pepper are mainly known for their antiobesogenic effects and have been shown to alleviate hepatic steatosis due to their interactions with genes related to lipid metabolism, such as peroxisome proliferator-activated receptors (PPAR) and carnitine palmi-toyltransferase1 (CPT1). However, the effect of chili peppers on maternal obesity models from a DOHaD perspective is currently unknown. We hypothesized that dietary intervention with chili pepper in a maternal obesity model can improve the metabolic health of mothers and their offspring.

Methods:
Before and during pregnancy, HFD female Wistar rats were intervened with capsiate-rich chili (Capsicum annuum L.) or capsaicin-rich chili (Capsicum chinense) at 100 mg/kg-feed of capsiate or capsaicin. Weight, MRI, liver Folch extraction, and liver rt-PCR were performed (M ± SEM, ANOVA, Analysis by unpaired t-test, α=0.05).

Results:
The addition of capsaicin-rich chili, but not capsiate-rich chili, significantly improved the metabolic health of obese pregnant rats, reducing maternal weight-gain, increasing lean mass and reducing the adiposity index and liver fat content by downregulating hepatic CPT1, without changes in PPAR-α and PPAR-γ. This prevented low fetal weight at day 19 of gestation, improved fetal liver weight and significantly reduced liver fat content in the offspring.

Conclusions:
Capsaicin-rich chili intervention prevents maternal obesity due to HFD, improving body composition and adiposity by intervening in the genetic expression of CPT1, reducing liver fat content. The mother's metabolic improvement resulted in an improved weight, liver weight, and liver fat content in offspring. Therefore, ingesting capsaicin-rich chili peppers could help prevent NALFD. However, clinical studies are needed to support these results.

Funding:
This research was supported by SECIHTI grant G-1176. VG-C acknowledges SECIHTI for her doctoral grant.

Key-words: (up to 5):
DOHaD; Capsaicin; Capsiate; obesity; nonalcoholic fatty liver disease

Abstract #00005748 en

Fetal growth restriction alters medial prefrontal cortex insulin sensitivity contributing to altered emotional responses via Wnt/β-catenin signaling pathway in females

Impact of Early Life Exposures and Environmental Pollutants

Maidana Miguel Patricia (1), Barth Barbara (1), Batra Aashita (1), Bonesso Alves Marcio (1), Mar Arcego Danusa (2), Alberry Bonnie (1), Dalle Molle Roberta (2), Gomez-Ilescas Ameyalli (1), Zhang Tie Yuan (2), Wen Xianglan (2), Parent Carine (2), O'Toole Nicholas (2), Krumel Portella Andre (2), Pelufo Silveira Patricia (1) (1) McGill University, (2) Douglas Research Centre

Background/aims:
Fetal growth restriction (FR) is associated with altered insulin sensitivity and increased risk for later psychiatric and metabolic disorders. This study investigated whether insulin infusion into the medial prefrontal cortex (mPFC) modulates behavioral responses to environmental cues in a sex-specific manner in adult rats exposed to FR. We also analyzed mPFC transcriptomic changes following peripheral insulin administration at key developmental stages.

Methods:
Pregnant Sprague Dawley dams were assigned to either a control (ad libitum-fed) or food-restricted group from gestational day 10. Offspring were tested at postnatal day (PND) 90 in the spontaneous alternation task (SAT) and light-dark box (LDB) following mPFC insulin injection 5 minutes before testing (n=5–12/group). mPFC RNA-sequencing was conducted after intraperitoneal insulin or saline administration at PND 0, 21, and 90 (n=10/group). All procedures followed institutional and national animal care guidelines (Ethics #DOUG-8018).

Results:
mPFC insulin infusion increased exploratory behavior in the SAT in males only, regardless of prenatal condition ($p<0.05$). In the LDB, insulin had an anxiolytic effect specific to FR animals of both sexes (adversity×treatment, $p<0.05$). Over time, insulin produced effects in the same direction in males, but opposing effects in Adlib vs. FR females (time×adversity×treatment, $p<0.05$). Transcriptomic analysis revealed stronger discordance between FR and FR insulin transcriptional signatures in females than males. Tmco3, a gene linked to physical growth and emotional response to environmental cues, was upregulated by insulin only in FR females (FDR<0.05). Pathway analysis identified Wnt/β-catenin signaling as a shared mechanism across FR and insulin conditions, especially in females (FDR<0.05). Developmental analyses revealed sex- and stage-specific gene expression, including early thyroid hormone alterations in FR insulin females.

Conclusions:
These findings show that mPFC insulin has sex- and condition-specific behavioral and molecular effects, with enhanced insulin responsiveness in FR females. This underscores the importance of sex as a biological variable in the context of early adversity.

Funding:
Natural Sciences and Engineering Research Council of Canada (NSERC #RGPIN-2018-05063)

Key-words: (up to 5):

fetal growth restriction, insulin, medial prefrontal cortex, anxiety-like behavior, RNA-seq

Abstract #00005749 en

Disrupted brain–adipose communication in female rats exposed to fetal growth restriction

Mechanisms Determining Transgenerational Effects of Health and Disease

Jaramillo Ospina Angela Marcela (1), Miguel Patricia Maidana (1), Alberry Bonnie (1), Pereira Laureano Daniela (2), Dalle Molle Roberta (3), Gómez Ilescas Ameyalli (1), Silveira Patricia Pelufo (1)
(1) McGill University, (2) Universidade Federal do Rio Grande do Sul, (3) Ludmer Centre for Neuroinformatics and Mental Health

Background/aims:
Poor fetal growth is associated with an increased preference for high-fat/high-sugar foods in humans, especially females, potentially contributing to elevated their risk for metabolic disease. Similarly, we showed that a rat model of poor fetal growth (FR; food restriction) displays comparable behavior and reduced dopamine release in the nucleus accumbens (NAcc) in response to sweet food. Brain´s dopaminergic system is highly influenced by peripheral metabolic context and chronic low-grade inflammation. For example, adiponectin, an anti-inflammatory cytokine secreted by adipocytes, crosses the blood-brain barrier to modulate dopaminergic neurons. The pro-inflammatory IL-1β is associated with dopaminergic neuron degeneration. Here, we investigated whether poor fetal growth alters these key peripheral regulators of brain dopaminergic neurotransmission and central dopamine transporter (DAT) levels, a critical regulator of striatal dopamine dynamics.

Methods:
Pregnant Sprague-Dawley rats were assigned to ad libitum feeding (Adl-control) or FR (50% food reduction) from gestational day 10 to 21. Offspring were fed ad libitum postnatally and sacrificed on postnatal day 90. Trunk blood, visceral fat (omental, gonadal, retroperitoneal), and whole brains were immediately collected. The NAcc was dissected, and DAT protein levels were measured by western blot. Plasma adiponectin (ng/mL) and IL-1β (pg/mL) were quantified using MILLIPLEX® kits (#RV2MAG-31K, #RADPKMAG-80K) on a Luminex® xMAP® platform. Group comparisons by sex were performed using Student's t-tests and multiple linear regression. All procedures followed ethical and animal welfare guidelines (Ethics Committee #DOUG-8018).

Results:
In females, prenatal FR had significantly higher plasma adiponectin and IL-1β, and lower DAT expression in the NAcc (all $P<0.05$), compared to Adl controls. No significant differences were observed between FR and Adl males (all $P>0.05$).

Conclusions:
These findings suggest that prenatal food restriction impairs brain–adipose communication in females, potentially linking inflammatory and adipokine alterations to dopaminergic regulation in the NAcc. Further research is needed to elucidate adiponectin's role under early-life adversity.

Funding:
Supported by the Canadian Institutes of Health Research (CIHR) and Postdoctoral Fellowship from the McGill-Douglas Max Planck Institute of Psychiatry International Collaborative Initiative in Adversity and Mental Health, an international partnership funded by the Canada First Research Excellence Fund, awarded to McGill University for the Healthy Brains for Healthy Lives initiative.

Key-words: (up to 5):

Nucleus accumbens, dopamine transporter, adiponectin, interleukin 1-beta, females

Abstract #00005750 en

Maternal Diet-Induced Obesity Alters Milk Caloric Content and Offspring Metabolism

Role of Infant and Young Child Feeding Practices on Long-Term Health

Rodrigues Aline Milena Dantas (1), Kipper Ana Caroline (1), Campos Mateus (1), Fabiane Isabelle (1), De Oliveira Júlio Cezar (1)
(1) Universidade Federal de Mato Grosso

Background/aims:
Obesity, recognized as a major disturbance in energy metabolism, can program metabolic dysfunctions in offspring when it occurs during critical stages of life. This study aims to assess breast milk caloric content, weight gain, and milk intake in male and female rat pups, and how these effects persist into adulthood after maternal high-calorie diet during lactation.

Methods:
Lactating Wistar rats were fed a high-calorie diet and 10% sucrose solution (Ob group), while control (Cont) received a standard diet. Pups were weighed every two days, and milk intake was measured on days of life 6, 11, and 16. Milk samples were collected on day 12 for biochemical analysis. Protocol by the ethics committee: 23108.017073-2019-56.

Results:
Ob-mothers display adiposity index 83.14% higher than Cont ($P<0.01$). Breastmilk calorie was 50.9% higher in Ob-mother than Cont. Regarding the pups, on the 6th day of life, Ob-male consumed 37.4% more milk than Cont, and Ob-female consumed 63.1% more than Cont ($P<0.001$). On the 11th day, Ob-male consumed 40.8% more, and Ob-female consumed 58.16% more than their counterparts ($P<0.05$). On the 16th day, Ob-male consumed 49.09% more ($P<0.001$), and Ob-female consumed 45.37% more than their counterparts ($P<0.01$). In relation to the counterparts, the pup's body weight was increased by 21.7% in Ob-male and 10% in Ob-female ($P<0.05$). Ob-male were 18.65% heavier than Ob-female ($P<0.001$), while there was no significant difference between Cont-male and Cont-female. ($P<0.05$). When comparing sexes, all groups showed statistically significant differences at both 60 and 120 days of life, when compared to the respective group of the opposite sex ($P<0.001$).

Conclusions:
High-calorie diet consumption by lactating mothers increases calorie-milk composition, which can influences male rat-offspring to develop hyperphagia and body weight gain earliest than female rat-offspring.

Funding:
Coordination for the Improvement of Higher Education Personnel (CAPES)

Key-words: (up to 5):
Lactation; Obesity; Metabolic programming

Abstract #00005752 en

Influence of Seasonality and Atmospheric Temperature on Pre-Eclampsia in Pregnant Women from Rio de Janeiro - Brazil

Effects of Environmental Climate Change on Early Life Health Setting in Future Generations.

Rezende Karina Bilda de Castro (1), Leitão Vitória Araujo (2), Grave Gabriela (2), Teixeira Valentina (2), Ladeira Luiza Paiva (2), Cardoso Maria Isabel (2), da Matta Fabio G (2), Almeida Aglaya Oliveira Cordeiro de (2)
(1) Maternidade Escola do Complexo Hospitalar da universidade Federal do Rio de Janeiro, (2) Maternidade Escola CH/UFRJ

Background/aims:
Preeclampsia(PE) is the leading cause of maternal and perinatal death in Brazil. This study aims to evaluate the influence of seasonality and daily atmospheric temperatures on conception and delivery on the occurrence of PE.

Methods:
A secondary analysis of women hospitalized for childbirth, in the biennia 2011-2012 and 2015-2016. The average, maximal, and minimal daily temperature (ADT, MaxDT and Min DT) on the estimated date of conception(EDC) and delivery were checked at https://portal.inmet.gov.br, against the records of the reference weather station at the place of residence. The local Ethics Committee approved the study (no
5.109.285)
The cases were categorized according to the month of delivery and conception. The respective prevalences of preterm and overall PE according to the delivery month were calculated and compared using the chi-square test with Bonferroni correction. The differences were considered significant with $p < 0.05$.

Results:
The sample comprised 7,954 deliveries. PE occurred in 617(7.7%) cases, with 176(2.2%) preterm PE. At the delivery date, the range of ADT was 13.65o- 33.28oC, MinDT was 8.6o - 29oC, and MaxDT was 17.4o42.2oC. Regarding the EDC, the range of ADT was 15.83o- 33.28oC, MinDT was 9.7o - 28.8oC, and MaxDT was 16.6o- 41.4oC. June recorded the lowest ADT. There were no differences in the occurrence of PE according to the month of delivery. The association between MinDT and ADT at delivery date was significant for preterm PE (p 0.003 and 0.04). Concerning the EDC, the ADT, MinDT, and MaxDT were significant for overall PE (p 0.017, 0.048 and 0.017).

Conclusions:
No seasonal variation was observed in preterm and overall PE across the years. However, the cases of preterm PE had a lower ADT and MinDT at the delivery date. Cases of overall PE were associated with the ADT, MinDT, and MaxDT of the EDC.

Funding:
Conselho Nacional de Desenvolvimento Científico e Tecnológico - Brasil

Key-words: (up to 5):
preeclampsia, seasons,temperature

Abstract #00005759 en

Alterations in the Composition of Fatty Acids and Protein in Colostrum and Transitional Breast Milk of Women with Gestational Diabetes

Role of Infant and Young Child Feeding Practices on Long-Term Health

Martínez-Ortega Larissa (1), Omaña-Guzman Isabel (2), Ibáñez-Chávez Carlos (1), Lozano-González Emilia (2), Méndez-Carballo Ana (2), Lanz-Pérez Luis (2), Jaramillo-Pimentel María (2), Alvarado-González Amhed (2), Ruiz-Barranco Alejandra (2), Cabrera-Aguilar Maria (2), Lomas-Soria Consuelo (1), Granados-Portillo Omar (1), Zambrano-González Elena (1), Garibay-Nieto Nayely (2)
(1) National Institute of Medical Sciences and Nutrition, "Salvador Zubiran", (2) General Hospital of Mexico, "Dr. Eduardo Liceaga"

Background/aims:
Gestational Diabetes Mellitus (GD) is a metabolic disorder characterized by glucose intolerance arising during pregnancy and may persist for up to 12 weeks postpartum. GD has been associated with abnormalities in breast milk composition, particularly in essential fatty acids and proteins, critical for infant neurological and metabolic development. Additionally, a pro-inflammatory profile has been observed in the breast milk of women with GD.The aim was to compare concentrations of polyunsaturated-fatty-acids and proteins in the breast milk of women with GD versus women without GD during the colostrum and transitional milk phases.

Methods:
A total of 71 breast milk samples (colostrum and transitional milk) were systematically collected from participants. This protocol was approved by Ethics and Research Committees (DI/24/303/05/3). Polyunsaturated fatty acid levels (omega-3 and omega-6) were analyzed using Gas-Chromatography. Protein concentrations were determined through fluorescence-based ELISA. Statistical comparisons between groups were performed using Student's t-test to assess mean differences. A p-value <0.05 was considered significant.

Results:
Colostrum from women with GD showed significantly lower protein concentrations compared to that from women without GD (3.8±0.4g/dL vs 5.2±0.5g/dL, p=0.02). No significant differences were observed in overall fatty acid profiles; however, transitional milk exhibited an upward trend in omega-6 levels in women with GD (336.6±58.6g/100g vs 222.4±25.4g/100g, p=0.06). Linoleic acid (257.3±56.4µg vs 158.5±20µg, p=0.06) and alpha-linolenic acid (19.3±1.8µg vs 25±1.1µg, p=0.02) levels differed significantly between groups. Protein concentrations in transitional milk were also lower in the GD group (1.4±0.2g/dL vs 2.2±0.2g/dL, p=0.02).

Conclusions:
GD significantly affects the nutritional quality of breast milk, particularly in essential fatty acid and protein composition. These increased omegna-6 concentrations in women with GD suggest a potential pro-inflammatory shift and highlight the necessity of tailored nutritional monitoring and intervention during pregnancy and lactation to support optimal maternal and infant health outcomes and epigenetic metabolic programming.

Funding:
SECTEI/149/2023

Key-words: (up to 5): BreastMilk,Gestational-Diabetes,Polyunsaturated-fatty-acids,Proteins.

Abstract #00005762 en

Increased Abundance of RECK in Placenta-Derived Extracellular Vesicles from Maternal Plasma in Preeclampsia: Anti-Angiogenic Effects and Induction of Common Symptoms in a Pregnant Mouse Model

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Gutierrez Jaime (1), Martinez Tomás (2), Rojas Felipe (2), Huang Xiu (2), Sergio Jiménez-Urrea Sergio (2), Leiva Andrea (1), Illanes Sebastian (3), Carvajal Jorge (4), San Martín Sebastián (5), Lazo Sofia (5), Gómez Isabel (2), Cantín Claudette (1)
(1) Universidad San Sebastian, (2) Universidad San Sebastián, (3) Universidad de Los Andes, (4) Pontificia Universidad Católica de Chile, (5) Universidad de Valparaíso

Background/aims:
Severe preeclampsia (sPE) is a pregnancy disorder characterized by maternal hypertension and multisystemic damage, increasing the long-term risk of cardiovascular, metabolic, and cognitive diseases for both mothers and their offspring. Its origin is linked to placental development defects during the first trimester, leading to the release of antiangiogenic factors and small extracellular vesicles (sEVs) into maternal circulation. Placental-derived sEVs (sEVs-PLAP) isolated from maternal plasma during the third trimester can induce PE-like symptoms in animal models; however, the specific vesicular cargo responsible remains unidentified. We propose that RECK, a protein with antiangiogenic properties elevated in sPE placentas, is enriched in sEVs-PLAP and may contribute to the antiangiogenic effects and clinical manifestations of sPE.

Methods:
sEV from maternal plasma of sPE and healthy pregnancies (HP) in the first, second and third trimester were purified by subsequent steps of size-exclusion chromatography, tangential flow filtration, and affinity chromatography. sEV were characterized by NTA, WB, TEM, and ELISA. The PE-promoting effect of sEV from placenta cells with overexpression or knockdown of RECK was assayed in vitro and in vivo.

Results:
sEVs from sPE and HP exhibit similar particle size distribution, morphology, and expression of exosome markers. However, both the number of sEV-PLAP in maternal plasma and the expression levels of RECK in these vesicles increased by 2.5-fold, nearly 10 weeks before the clinical diagnosis of sPE. Placenta-derived sEVs with elevated RECK levels impaired angiogenesis in vitro through a mechanism involving the inhibition of metalloproteinase activity. In vivo, sEVs enriched in RECK induced characteristic symptoms of sPE in pregnant mice, including maternal hypertension, proteinuria, and intrauterine growth restriction in the offspring

Conclusions:
RECK is augmented in sEVs-PLAP present in the maternal plasma prior to the diagnosis of sPE. RECK in sEVs play key roles in the origin and development of sPE and also emerge as a biomarker of sPE.

Funding:
FONDECYT 1221362 (Chile)

Key-words: (up to 5): Preeclampsia, Extracellular Vesicles, RECK, Angiogenesis

Abstract #00005765 en

Effect of maternal or infant probiotic supplementation on multiple food allergies: a systematic review of randomized controlled trials

Role of Infant and Young Child Feeding Practices on Long-Term Health

Badin Rebeka Caribe (1), Figueira Priscila Helena Marietto (2), Pereira Vivian do Nascimento (3), Alves Manaças Liliane Rosa (4)
(1) Fametro/INCA/HUGV/UFAM, (2) INCA, (3) HUGV/UFAM, (4) INCA/UFRJ

Background/aims:
Animal model studies have demonstrated the benefits of probiotic use during pregnancy and the early years of offspring in preventing food allergies and promoting tolerance. However, in human studies, the effectiveness remains uncertain. Given the lack of scientific consensus, this review aimed to evaluate the effects of maternal or infant probiotic supplementation on the risk of developing multiple food allergies.

Methods:
A systematic search was conducted in the MEDLINE/PUBMED, LILACS, and SciELO databases to identify studies evaluating the impact of probiotic supplementation on the development of food allergies. The strategy for including studies followed the PICOS criteria: Participants (human studies), Interventions (probiotic supplementation during pregnancy or infancy), Comparisons (with or without probiotic supplementation), Outcomes (occurrence or tolerance of food allergies in children with food allergies or healthy children), and Study design (randomized controlled trials). The inclusion criteria for the studies were as follows: studies available in full text, published between 2019 and March 2025. Two independent reviewers were responsible for data extraction and synthesis.

Results:
A total of 1,504 articles were retrieved through the search strategies, with an additional 2 records identified through other sources. After screening, 5 trials on probiotic supplementation for food allergies were included: 2 focused on cow's milk allergy, 1 on peanut allergy, and the remaining trials addressed general food allergies. The RCTs included 1,283 participants, with 613 in the probiotic supplementation group and 670 in the control group. Geographically, 60% of the studies were conducted in Europe and Asia, and 40% in Oceania.

Conclusions:
This systematic review suggests that probiotic supplementation may offer potential benefits for children with food allergies. Nevertheless, the variability in study outcomes undermines the strength of the evidence. Consequently, larger clinical trials with more diverse participant groups and standardized methodologies are needed to more conclusively establish the efficacy of this intervention.

Funding:
No funding was received for this research.

Key-words: (up to 5):
probiotics, pregnancy, infancy, food allergies

Abstract #00005772 en

Cardiovascular Risks of Prenatal Cadmium Exposure

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Zhang Kurt (1), Xie Linglin (2)
(1) Texas A&M Health Science Center, (2) Texas A&M Agrilife Research

Background/aims:
Congenital heart defects (CHDs) are the most common birth defects and are the leading cause of morbidity and mortality in infants and children. Of these, left ventricular hypertrabeculation (LVHT) is a heart defect that is presumably the result of an incomplete compaction process and myocardial hyperplasia. Cadmium (Cd), a natural heavy metal and environmental contaminant concentrated by industrial activity, is an etiological factor in carcinogenesis, renal dysfunction, and cardiovascular disease. Moreover, prenatal exposure to this metal has been shown to alter heart development and be significantly associated with the incidence of heart defects.

Methods:
C57BL/6 female mice either were orally dosed with Cd through their drinking water, at a concentration of 50mg/L, from one week preconception through the duration of their pregnancy, or served as controls. Pregnant female mice were sacrificed at E12.5 or E14.5, and the embryos were collected for histological and molecular examination. Additionally, a germline knockdown of Gata4 was generated, and the mice were prenatally exposed to Cd.

Results:
Prenatal Cd exposure was found to induce ventricular hypertrabeculation in the developing embryo, which was accompanied by significant myocardial hyperplasia. Consistently, upregulation of mRNA and protein levels were observed in the genes known to impact cardiomyocyte proliferation, such as p-AKT and Gata4. Furthermore, the Gata4 mutants demonstrated a phenotypic rescue of hypertrabeculation upon Cd treatment.

Conclusions:
These results suggest the important role of the Gata4-PI3K axis in Cd induced LVHT. In summary, this study generates an excellent mouse model for studying ventricular development, and provides compelling evidence for a genetic-environmental interaction underlying the pathogenesis of hypertrabeculation.

Funding:
This study was supported by NIH/NIEHS P30ES029067.

Key-words: (up to 5):
Cadmium, congenital heart defect, left ventricular hypertrabeculation

Abstract #00005776 en

Impact of maternal overweight and butyrate treatment in liver lipid lipogenesis

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Heinecke Florencia (1), Dechamps Victoria (2), Labiano Marina (2), Flores Quiroga Jermías Pablo (2), Galarza Rocío Alejandra (3), White Verónica (2)
(1) CEFYBO-CONCIET-UBA, (2) CEFYBO-CONICET-UBA, (3) CEREGGeo-FCyT-UADER, Facultad de Ciencia y Tecnología, Universidad Autónoma de Entre Rios

Background/aims:
We previously observed maternal hypertriglyceridemia, fetal overweight and liver lipid overaccumulation in mothers and offspring in a rat model of maternal overweight. Butyrate, a short-chain fatty acid from fiber metabolism by intestinal microbiota, improves lipid metabolism and prevents inflammation. Maternal butyrate administration prevented hypertriglyceridemia, fetal overweight and liver lipid overaccumulation in offspring, but not in mothers.
Aim: To evaluate whether liver lipogenesis and its key regulators were disturbed by maternal overweight and/or modulated by butyrate treatment.

Methods:
Female Wistar rats were fed standard (CT) or high-fat (FD) diet for 8 weeks and mated with CT males. Butyrate (3%) or vehicle was orally administered daily during gestation and three times per week during lactation (FDB). Pregnant rats and their fetuses were euthanized at gestational day 21. Other mothers were euthanized after weaning and offspring at 140 days. Hepatic mRNA levels of lipid homeostasis regulators were assessed by RT-qPCR.

Results:
Term-gestating rats showed increased liver Srebp-1c mRNA levels in the FDB group(41%), negatively correlating with triglyceridemia (Pearson-R: -0.4935). Fetal liver Srebp-1c mRNA levels were increased in FD group(60%) and prevented by butyrate only in female fetuses. After weaning, liver Srebp-1c increased in both FD and FDB mothers (106%), negatively correlating with triglyceridemia (Pearson-R: -0.7026) and positively with adipose tissue weight (Pearson-R: 0.5565). In female offspring Srebp-1c and Lrxa mRNA levels were increased in FD (120%) and prevented by butyrate, while in male offspring, Srebp-1c mRNA levels were decreased in both FD and FDB groups (56%), with no changes in Lrxa mRNA.

Conclusions:
Maternal butyrate treatment showed beneficial but distinct effects: in mothers, it increased lipid overaccumulation, possibly through upregulation of Srebp-1c. In offspring, it prevented liver lipid accumulation, probably in females through downregulation of Srebp-1c and Lxra with unknown mechanisms in males. This highlights the importance of considering sex as a biological variable in metabolic programming.

Funding:
PICT-2020-Serie-A-nº-01125/ PICT-2021-nº-I-A-00381-PIP 2022/2024 CONICET. Ethical Approval:

CICUAL-n°3001-2022. The authors state that they have no conflicts of interest.

Key-words: (up to 5):
Maternal overweight - Butyrate intervention - Intrauterine programming - Lipogenesis

Abstract #00005778 en

Effect of the proportion of pregestational and gestational dietary linoleic acid intake on female fetal development

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Gómez-Cayupán Jorge (1), López Angelica (1), Flores Cristian (1), Barrera Cynthia (1), Maliqueo Manuel (1)
(1) Endocrinology and Metabolism Laboratory, West Division, School of Medicine, University of Chile.

Background/aims:
Pregestational obesity (PGO) increases the risk of metabolic and reproductive diseases in offspring in a sex-dependent manner. Additionally, dietary intake of fatty acids, such as saturated fatty acids (SFAs) and n-6 polyunsaturated fatty acids (PUFAs), has been shown to negatively impact fetal development.
However, the effect of their combination on the offspring remains unclear.

Methods:
During 10 weeks, twelve-week-old C57/BL6 female mice were fed either a control diet (CD) (10% kcal fat) containing low (1,6%), medium (2.8%) or high (4%) kcal of linoleic acid (LA), or a high fat diet (HFD) (45% kcal fat) containing low (5.5%), medium (9.6%) or high (13.7%) kcal of LA. Then, they were mated and maintained with experimental diets until delivery. Biometric analysis in the female offspring for metabolic and reproductive alterations was performed at postnatal days (pnd) 7 and 21. Data were analyzed using 2-way ANOVA. The Institutional Ethics Committee for the care and use of animals of the University of Chile approved the protocols (#CBA-1304).

Results:
At pnd 7, the offspring of mice fed with medium LA showed increased body length compared to low- and high-LA intake, regardless of kcal fat content. Anogenital distance at pnd 7 and body weight at pnd 21 were also higher in the medium-LA group than in the high-LA group, but not in the low-LA group in the HFD group.

Conclusions:
Proportions of dietary n-6 PUFAs may affect fetal development, as a medium-LA diet may interact with SFAs more efficiently than a low- or high-LA diet, causing increased size, weight, and AGD in the offspring. These results suggest that an unbalanced pregestational and gestational intake of n-6 PUFAs may negatively impact metabolic and reproductive development, as often seen in some PGO models.

Funding:
FONDECYT 1241725

Key-words: (up to 5):
Linoleic acid, Pregestational obesity, Fetal development.

Abstract #00005779 en

Fructose Exposure during Development Alters Neural Progenitor Cell Proliferation and Neuron-Astrocyte Differentiation: Increased Sensitivity during Fetal Life

Mechanisms Determining Transgenerational Effects of Health and Disease

Baqueiro Mayara (1), Costa Suleyma (1), Han Guang (2), Bora Lihiri (2), Hernandez Jacqueline (2), Torsoni Marcio (3), Ross Michael (2), Torsoni Adriana (3), Desai Mina (2)
(1) University of Campinas (UNICAMP) / The Lundquist Institute at Harbor-UCLA , (2) The Lundquist Institute at Harbor-UCLA Medical Center, (3) University of Campinas (UNICAMP)

Background/aims:
Excessive fructose consumption is commonplace in Western diets and represents a significant contributor to development of obesity. The recent increase in maternal obesity has coincided with a marked rise in the rate of childhood neurodevelopmental disorders. The hippocampus has a key role in learning and memory, and hippocampal dysfunction has been associated with neurobehavioral abnormalities. We hypothesized that fructose exposure may have adverse impact on hippocampal neurodevelopment during fetal and newborn life. This study aimed to assess the effects of fructose treatment in vitro on neural progenitor cell (NPC) proliferation and differentiation at two key developmental stages: embryonic day 12.5 (E12.5) and postnatal day 3 (p3).

Methods:
Central nervous system NPCs were obtained from mice embryos at e12.5 (C57BL/6, MUBNF-01101) and hippocampal-specific NPCs obtained from newborn mice (day 3 of life, n=36). NPC cultures were established in complete medium and subsequently differentiated in presence or absence of low or high dose D-fructose (5, 12.5 mM). After 5 days differentiation, astrocytes (GFAP) and neurons (NeuN, MAP2) were counted by immunofluorescence using ImageJ Software. t-test or ANOVA was used ($p<0.05$).

Results:
In neonatal cells, 12.5 mM fructose increased NPCs proliferation vs controls (0.91±0.18 vs 0.47±0.21, $p<0.01$). When differentiated, embryo NPCs reduced neuron/astrocyte ratio when exposed to 5mM (1.4±0.1 vs 1.9±0.1, $p=0.02$) or 12.5mM D-fructose (1.5±0.1 vs 1.9±0.1, $p=0.02$). Similarly, in neonatal NPCs, 12.5 mM fructose decreased neuron/astrocyte ratio (2.5±0.1 vs 3.8±0.4, $p=0.04$), though there was no change in response to 5mM fructose.

Conclusions:
In vitro findings indicate that prenatal and early postnatal fructose exposure reduces the hippocampal neuron/astrocyte balance, with an increased sensitivity during fetal life. Excess gliogenesis vs neurogenesis may result in impaired cognitive function later in life. Our findings highlight the need to limit maternal high-fructose/sucrose intake during pregnancy/lactation and support stricter sweetener regulation in infant formula.

Funding:
NIH grant #R01HD099813

Key-words: (up to 5):
Fructose, Hippocampus, Offspring, Sugar.

Abstract #00005781 en

Childhood and Adolescent Body Mass Index as a Risk Factor for Endometrial Cancer: A Systematic Review

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Manaças Liliane Rosa Alves (1), Marietto Figueira Priscila Helena (2), Oliveira Mariana Borges (3), Badin Rebeka Alves Caribé (4)

(1) Universidade Federal do Rio de Janeiro - UFRJ, Instituto Nacional de Câncer - INCA, (2) Instituto Nacional de Câncer - INCA, (3) Hospital Municipal Miguel Couto, (4) Instituto Nacional de Câncer - INCA, HUGV/UFAM

Background/aims:

Endometrial cancer (EC) is the seventh most common cancer among women. Although adult obesity is a well-established risk factor, the impact of early-life adiposity on EC risk is less clear. This systematic review aimed to evaluate the association between childhood and adolescent body mass index (BMI) and the development of EC in adulthood.

Methods:

A systematic search was conducted in the MEDLINE (PubMed), LILACS, and SciELO databases for studies published between March 2015 and February 2025. Using PECO criteria, the population was individuals aged 0–19 years; the exposure was elevated BMI during childhood or adolescence; the comparator was normal BMI; and the outcome was the development of EC in adulthood. Study selection and data extraction were performed independently by two reviewers.

Results:

A total of 90 records were identified, including 30 observational studies. After full-text screening of 14 articles, five studies met the inclusion criteria. All included studies were cohort studies conducted in South America or Europe, with sample sizes ranging from 1,765 to 162,559 participants. One study assessed BMI at birth and found no association with EC risk, while the others identified a positive association between elevated early-life BMI and an increased EC risk. However, three studies reported that this association was no longer statistically significant after adjusting for BMI at diagnosis. Additionally, 40% of the studies stratified results by histological subtype, showing weaker associations with non-estrogen-dependent endometrial cancers.

Conclusions:

Although evidence remains limited, elevated BMI from childhood through adulthood appears to play a significant role in EC development. Maintaining a healthy weight across all life stages may be crucial for EC prevention, and interventions targeting adiposity early in life could help reduce the risk of specific EC subtypes.

Funding:

No funding was received for this research.

Key-words: (up to 5):

Endometrial cancer, Body mass index, Childhood

Abstract #00005786 en

Small litter size rewires gut microbiota and SCFA networks under high-sucrose challenge

Role of Infant and Young Child Feeding Practices on Long-Term Health

Martins Silva Ana Flávia (1), Rezende Ribeiro de Abreu Aline (1), Neves Freitas Nicolly (1), Jesus de Deus Isabela (1), Martins de Andrade Fagundes Miliane (2), Rosse Izinara (3), Ângelo Gonçalves de Moraes Lauro (4), Silveira Breguez Gustavo (1), Bearzoti Eduardo (5), Dutra Medeiros Julliane (6), Ariston de Carvalho Azevedo Vasco (7), Góes Neto Aristóteles (8), Guerra de Sá Renata (9), Barbosa de Queiroz Karina (2)

(1) Postgraduate Program in Health and Nutrition, Federal University of Ouro Preto, (2) Department of Food, Federal University of Ouro Preto, (3) Department of Pharmacy, Federal University of Ouro Preto, (4) Research Center in Biological Sciences/NUPEB, Federal University of Ouro Preto, (5) Department of Statistic, Federal University of Ouro Preto, (6) Department of Biology, Federal University of Juiz de Fora, (7) Department of Biological Genetic, Federal University of Minas Gerais, (8) Department of Microbiology, Federal University of Minas Gerais, (9) Department of Biological Science, Federal University of Ouro Preto

Background/aims:

The DOHaD concept emphasizes how early-life nutritional exposures can program long-term metabolic health. Gut microbiota perturbations during critical windows, particularly around lactation, have lasting effects on host metabolism, immunity, and neurodevelopment, partly through microbially derived SCFA. Dietary substrates shape distinct bacterial signatures, while high-sucrose diets (HSD) promote dysbiosis. Here, we explore how small litter size (SL) interacts with HSD to influence gut microbiota composition, SCFA production, and microbial network architecture. We aim to determine whether the SL offers some degree of resilience against these dietary challenges.

Methods:

After birth, male Wistar rats (n=29) were randomly divided into control (CL, 8 pups/dam) and small litter (SL, 4 pups/dam) groups. At 21 days, the animals were weaned and redistributed into four diet-based groups: standard (STD) or high-sucrose (HSD, 30% sucrose). After 8 weeks on these diets, the animals were euthanized, and cecal content was collected for 16S rRNA sequencing and SCFA quantification.

Approved by CEUA/UFOP (2245040518).

Results:

The HSD reduced gut microbial alpha and beta diversity in CL animals ($P < 0.05$), and increased Firmicutes/Bacteroidotes ratio ($P < 0.05$). However, SL animals showed no such changes despite exposure to HSD. LEfSe analysis revealed that SL animals on HSD were enriched in Subdoligranulum sp., Monoglobus sp., Allobaculum sp., and Escherichia–Shigella sp. Meanwhile, under STD they exhibited an increased abundance of Bacteroides pectinophilus group. HSD-SL animals showed the highest fecal SCFA concentrations, indicating enhanced fermentative activity ($p<0.05$). Co-occurrence network analysis revealed that the HSD-SL group had the most complex and densely connected microbial-functional network, indicating that HSD and SL synergistically reorganize SCFA-producing microbial–functional networks.

Conclusions:

These findings suggest that SL-induced metabolic imprinting enhances the resilience and functional organization of gut microbiota, emphasizing early-life interventions as a promising approach to mitigate metabolic diseases.

Funding:

CAPES 001, FAPEMIG APQ-02200-21, BDP-00094-22, RED00132-16, APQ-02511-22, APQ-04983-22, Finep e UFOP.

Key-words: (up to 5):
small litter size; gut microbial signature; DOHaD; short-chain fatty acids, high-sucrose diet

Abstract #00005789 en

Early pregnancy HbA1c based composite risk score is associated with higher new-born adiposity in Indian boys and not girls

Big Data and Cohorts in DOHaD Research.

Saravanan P (1), Ghebremichael-Weldeselassie Yonas (2), Mohan D (3), Anjana RM (4), Asres H (2), Surapaneni T (5), Kallur SD (5), Sukumar N (1), Mohan V (6), Ram U (7)

(1) Warwick Academic Health, Warwick Medical School, University of Warwick, Coventry, UK , (2) School of Mathematics and Statistics, The Open University, UK , (3) Madras Diabetes Research Foundation, Chennai, India, (4) Madras Diabetes Research Foundation, Dr Mohan's Diabetes Specialties Centre, Chennai, India, (5) Fernandez Hospitals, Hyderabad, India, (6) Madras Diabetes Research Foundation, India; Dr Mohan's Diabetes Specialties Centre, Chennai, India , (7) Seethapathy Clinic and Hospital, Chennai, India; Fetal Care research Foundation, Chennai, India

Background/aims:

Early pregnancy HbA1c has been shown to be associated with adverse birth outcomes. We examined the sex-specific association of HbA1c based composite risk score (age, BMI, family history of diabetes and HbA1c) in early pregnancy with neonatal adiposity in the STRiDE-India cohort.

Methods:

STRiDE-India was a prospective cohort study (n=2115), which showed that a novel early pregnancy composite risk score can help risk stratification (high, medium and low) with a potential to avoid the need for oral glucose tolerance test (OGTT). A sub-study sample (n=968; GDM-17.4%) of STRiDE-India cohort had neonatal adiposity calculated using subscapular and triceps skinfold thicknesses at birth. Regression analysis was carried out to test the composite risk score categories [high (27.1%), medium (52.7%) and low (20.2%)] with sex-specific neonatal adiposity, adjusted for parity, GDM treatment, gestational age at delivery and birth weight. GDM was diagnosed by International Association of Diabetes and Pregnancy Study Group (IADPSG) criteria.

Results:

Total neonatal adiposity was similar between babies born to women diagnosed as GDM or non-GDM by OGTT at 24-28 weeks. However, by STRiDE composite risk score, neonatal adiposity was higher in both high (β=1.71; 95%CI: 0.85,2.57; p<0.001) and medium (β=1.57; 95%CI: 0.82,2.31; p<0.001) categories as compared to low-risk category. In addition, these were present only in boys but not in girls: boys born to high-risk group: β=2.48; 95%CI: 1.35, 3.6; p<0.001; medium risk group: β=2.05; 95%CI: 1.04, 3.05; p<0.001. In girls, these were β=0.75; 95%CI: -0.53, 2.02; p=ns, and β=0.98; 95%CI: -0.12, 2.07; p=ns, respectively.

Conclusions:

HbA1c based composite risk score in early pregnancy may identify new-born with higher adiposity at birth in Indians. The sex-specific association may be due differences in adverse intrauterine programming between gender. Whether these differences persist in later life or related to the future metabolic risk in the offspring will require follow-up studies.

Funding:

Medical Research Council, UK; Department of Biotechnology, India; Open Societal Challenge Fund the Open University, Milton Keynes, UK

Key-words: (up to 5):
Gestational Diabetes, Neonatal adiposity, Composite risk score, HbA1c

Abstract #00005790 en

Enhancing Public Understanding of DOHaD to Inform Health Policy in New Zealand

Public Health Policies Across the Life Cycle.

Hildreth Jillian (1), Bay Jacquie (1)
(1) Liggins Institute, University of Auckland

Background/aims:
DOHaD evidence indicates that environmental influences during early development shape an individual's trajectory towards NCDs in later life. This has profound implications for health, prompting institutions such as the World Health Organization and the World Bank to integrate DOHaD-informed frameworks into global health agendas. Despite such high-level endorsement, poor understanding of DOHaD principles amongst the NZ public, coupled with a strong belief in health as an individual lifestyle choice, restricts introduction of meaningful policy changes at a national level. Without pressure from a well-informed public, decision-makers lack the mandate or incentive to address race-based inequities and other structural contributors to lifelong health.

Methods:
Drawing on methods from deliberative democracy, two small-scale workshops were conducted with NZ adults (women-only, n=18, men-only, n=12). Participants from diverse educational, ethnic, and parenting backgrounds were introduced to DOHaD evidence and supported to explore the concept of developmental plasticity. Groups discussed the relevance of DOHaD knowledge for public health in NZ and strategies for dissemination in the wider community. Thematic analysis was used to identify patterns in the data. Ethics:
UAHPEC #25369.

Results:
Participants recognised the significance of DOHaD for NZ communities, identifying a need for both public education and political action to promote healthy early-life development and positive long-term health outcomes. Informal interpersonal dialogue was identified as a key factor in building public awareness, to bring DOHaD evidence into more "mainstream" societal conversations. In response, a science communication resource was developed with the aim of introducing epigenetics concepts to NZers in a user-friendly and highly shareable format.

Conclusions:
Although awareness in NZ adults is low, those exposed to DOHaD evidence agree on its relevance for informing policy, underscored by the necessity for more widespread education around DOHaD concepts. A new resource aims to address this need.

Funding:
JH is supported by a University of Auckland Doctoral Scholarship.

Key-words: (up to 5):
DOHaD knowledge translation, public understanding, community engagement, public health policy, science communication

Abstract #00005792 en

Consumption of capsiate (Capsicum annuum L.) or capsaicin (Capsicum Chinense) ameliorates morphometric and biochemical parameters in obese pregnant rats

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Granados Higa Gabriela Elizabeth (1), García Morales Abigail (1), Ibáñez Chávez Carlos (2), Vega Nicolás Felipe De Jesús (2), Rodríguez González Leticia Guadalupe (2), Lomas Soria María Del Consuelo (2) (1) Universidad Autónoma Metropolitana/ INCMNSZ, (2) INCMNSZ

Background/aims:
Gestational obesity (GO) has implications for the mother and the fetus. Maternal metabolism and nutrition play a fundamental role in placental morphology and proper fetal development. Alternatives that mitigate the negative effects of GO are necessary. Compounds such as capsiate and capsaicin (present in chili peppers) promote body fat mobilization, weight loss and ameliorates metabolic effects caused by obesity. However, studies that analyzing the effect of chili peppers on GO are scare. The present study, analyses the effect of chili peppers intervention on maternal morphological, metabolic parameters, placental and fetal

Methods:
Female Wistar rats were weaned on to control (C) or high fat diet (MO), until 19 days of gestation. One of the MO groups was supplemented with capsiate (MOC100) or capsaicine (MOH100) from 90 days until 19 days of gestation at 100 mg/kg. At 19dG all groups were euthanized and serum, adipose tissue, placenta and fetus were collected. Placental fat by Folch and triglycerides were performed. P value <0.05 M± SE,
ANOVA

Results:
MOC100 and MOH100 showed reduced body weight gain, body fat, adiposity index, and lower insulin resistance compared to MO. At placental level, MO showed lower weight, higher fat and triglycerides content vs C. MO fetuses had lower weight than the C. Interestingly, MOC100 and MOH100 present values similar weight to C. However, for female placenta, MOH100 group showed lower fat and triglyceride levels than MO and MOC100, having fetus with weights similar to those of C

Conclusions:
Consumption of capsiate-or capsaicin-rich chili peppers in MO mothers mitigates the increase in body weight and adipose tissue compared to MO without intervention. Furthermore, these compounds prevent the lower weight in fetus, showed similar values than C. We can infer that these components counteract the adverse effects of maternal obesity on the mother and her fetuses

Funding:
This work was supported by CONAHCyT grant G-1176

Key-words: (up to 5):
Maternal obesity, capsiate, capsaicin, morphometric, placenta

Abstract #00005794 en

Linoleic acid (LA) intake, metabolic profile, and neonatal outcomes in pregnant women. Preliminary results.

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Villablanca Claudia (1), Ortiz Macarena (2), Sanchez Francisca (2), Valenzuela Rodrigo (2), Maliqueo Manuel (2) (1) Universidad de Chile, (2) Laboratory of Endocrinology and Metabolism, Faculty of Medicine, Universidad de Chile

Background/aims:
The western diet is currently characterized by a high consumption of soybean and sunflower oil rich in n-6 polyunsaturated fatty acids (PUFA), mainly linoleic acid (LA). Pregnancy could be a period susceptible to dietary factors, such as high intake of n-6 PUFA, since these are metabolized to proinflammatory derivatives that could increase the risk of developing pregnancy pathologies and alterations in anthropometric parameters of the newborn. However, this population has not been extensively studied for the effects of an excessive intake of n-6 PUFA. Therefore, this study evaluated the relationship between LA intake during the third trimester of gestation with maternal clinical, biochemical, and anthropometric parameters of the newborn.

Methods:
Forty-four pregnant women underwent a dietary survey and a blood sample to measure glycemia, lipid, and hepatic profile at the end of gestation. Delivery data and anthropometric parameters of the NB were obtained. LA intake was divided into tertiles, and differences between groups were analyzed by one-way ANOVA followed by Dunnet's test. Participants gave written consent to the protocol approved by the CEISH of the Faculty of Medicine of the University of Chile (protocol N° 201-2017 y 236-2020) and the Western Metropolitan Health Service (letter 20).

Results:
Pregnant women with higher LA intakes (tertile 3) had higher glycemia and albumin levels compared to the first tertile ($P < 0.05$). Length in NB was lower in tertile 2 compared to tertile 1 ($P < 0.05$). No differences were observed in maternal BMI and blood pressure.

Conclusions:
The results suggest a possible effect of higher intakes of LA on maternal glycemia, which would put pregnant women at greater risk of developing gestational diabetes. Other metabolic markers and the impact of LA derivatives during gestation need to be evaluated.

Funding:
FONDECYT 1181798 - 1241725, Laboratory of Endocrinology and Metabolism, School of Medicine,
University of Chile.

Key-words: (up to 5):
Linoleic acid, pregnancy.

Abstract #00005796 en

Gestational weight gain (GWG) should be optimized by age and Asia-Pacific BMI categories.

Big Data and Cohorts in DOHaD Research.

Ram U (1), Asres H (2), Thirunavukkarasu M (3), S Nishanth (3), Sukumar N (4), Saravanan P (4), Ghebremichael-Weldeselassie Yonas (5)

(1) Seethapathy Clinic and Hospital, Chennai, India; Fetal Care research Foundation, Chennai, India , (2) School of Mathematics and Statistics, The Open University, Milton Keynes, UK , (3) Seethapathy Clinic and Hospital, Chennai, India , (4) Warwick Academic Health, Warwick Medical School, University of Warwick, UK , (5) School of Mathematics and Statistics, The Open University, UK

Background/aims:
Current IOM GWG recommendations are not Age- or population-specific. This study aimed to assess whether age and South Asia (SA)-specific BMI thresholds based GWG guidelines will provide better healthy pregnancy (HP) outcomes.

Methods:
Data from a cohort of 13,870 singleton live births at two maternity hospitals in Chennai, India were analyzed, excluding women with pre-existing diabetes or hypertension. HP was defined as a live birth without prematurity or emergency cesarean, and with appropriate-for-gestational-age (AGA) birthweight, outcomes potentially causally related to GWG per IOM recommendations. The new GWG interval were obtained using harmonic mean (HM) scoring and statistical significance testing, comparing the odds of HP outcomes within versus outside appropriate GWG interval, adjusting for parity and gestational diabetes.

Results:
Age and BMI were independently associated with HP outcomes (age: OR=0.97, 95%CI: 0.96–0.98, BMI: OR=0.95, 95%CI: 0.94–0.95, both $p<0.001$). The new GWG guidelines were more precise than IOM. For example, in obese women (IOM:5-9kg), age-specific new guidelines were 18–25years: 6.6-12.6, 26–30years: 5.4-11.4 and >30years: -4.8 to -2.8kg. Women gaining GWG within the new ranges had higher HP rates, across all age and BMI categories, compared to IOM guidelines (18-25years: New:64.45% vs. IOM: 55.41%, 61.09% vs. 58.13%, 57.43% vs. 42.53%; 26-30years: 61.34% vs. 55.41%, 58.19% vs. 55.11%, 54.24% vs. 54.47%; >30years: 59.05% vs. 55.7%, 67.92% vs. 54.19%, 92.86% vs. 49.69% for normal, overweight, and obese categories). After multiple testing correction, the HP rates in normal BMI women aged 26–30, obese women aged 18–25 and 31–40 years remained significant, $p\leq 0.03$.

Conclusions:
Stratifying GWG recommendations by maternal age and population-specific BMI may contribute to achieve better HP outcomes in Indian women. Whether this applies to other populations requires validation studies.

Funding:
School of Mathematics and Statistics, The Open University; Open Societal Challenge Fund, The Open University, Milton Keynes, UK.

Key-words: (up to 5):
Gestational weight gain, IOM guidelines, South-Asian population, pregnancy outcomes

Physical Activity; Cardiometabolic Risk Factors; Longitudinal studies; Lifestyle.

Abstract #00005808 en

Maternal resistin levels and placental resistin-CAP1 association influence neonatal body composition.

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Molerés Orduña Miranda Adriana (1), Antonides Jensen Natalia (2), Arceo Cerna Carla (1), Castillo Santos Andrea Ofelia (1), Valencia Ortega Jorge (3), Perichart Perera Otilia (1), Estrada Gutierrez Guadalupe (1), Hernandez Sonia
(4), Solis Paredes Juan Mario (1)
(1) Instituto Nacional de Perinatología , (2) University of Chicago, Chicago, USA, (3) Hospital Infantil de México “Federico Gómez”, (4)

Background/aims:
Resistin, a proinflammatory cytokine involved in metabolic and immune functions, is secreted by multiple cell types, including the placenta. However, its relationship with maternal nutritional status and neonatal body composition remains poorly understood. Moreover, Cyclase Associated Actin Cytoskeleton Regulatory Protein 1 (CAP1), a known resistin receptor, has not previously been characterized in human placental tissue. Understanding the localization and functional associations of resistin and CAP1 could shed light on mechanisms of fetal programming.

Methods:
We enrolled 37 healthy mother–infant dyads from the OBESO cohort at INPer (ethics approval: 2024-1-14). Maternal pregestational BMI was calculated in the first trimester according to WHO criteria, and gestational weight gain was considered. Maternal serum resistin concentrations were measured by ELISA across trimesters. Placental resistin and CAP1 expression were assessed by immunostaining of paraffin-embedded sections. Analyses were performed across normal weight, overweight, and obesity groups. Differences were assessed by the Kruskal–Wallis test with Bonferroni correction, and correlations were evaluated using Spearman correlation. Analyses were conducted using STATA v.14, with $p<0.05$ considered statistically significant.

Results:
Placental resistin levels were significantly lower in the obesity group compared to normal weight group ($\rho = .014$). Second-trimester maternal resistin levels positively correlated with neonatal length ($\rho = .496$; $p = .026$). In normal weight pregnancies, placental CAP1 expression positively correlated with neonatal abdominal circumference ($\rho = .558$; $p = .020$) and neonatal length ($\rho = .749$; $p = .017$); these associations were not observed in the obesity group. Immunostaining revealed broad CAP1 expression in maternal and fetal placental cells, whereas resistin localized specifically to $CAP1^{+}$ macrophages in the maternal circulation.

Conclusions:
Maternal and placental resistin levels, together with the newly described CAP1 placental expression, are associated with neonatal body composition, suggesting a potential role in fetal programming modulated by maternal nutritional status.

Funding:
Kiphart Scholars

Key-words: (up to 5):
Resistin, Placenta, CAP1,

Abstract #00005820 en

High urine levels of endocrine disruptors in pregnant Mexican women and its association with phenotypic changes related to immune blood cell activation in both mothers and newborns

Impact of Early Life Exposures and Environmental Pollutants

Martínez Ibarra Alejandra (1), González-Sánchez Ignacio (2), Coronado Zarco Alejandra (3), Arreola Ramírez Gabriela (4), Martínez-Razo Luis Daniel (5), Cerbón Marco (6), Mancilla Herrera Ismael (3)
(1) Universidad Nacional Autónoma de México Facultad de Química, (2) Hospital General Dr. Manuel Gea González Departamento de Investigación Biomédica, (3) Instituto Nacional de Perinatología Isidro Espinosa de los Reyes, (4) Instituto Nacional de Pelinatología Isidro Espinosa de los Reyes, (5) Hospital General de México Servicio de Genética, (6) Universidad Nacional Autónoma de México, Facultad de Química

Background/aims:
The human population is unintentionally and daily exposed to endocrine disrupting compounds (EDCs), which induce molecular and functional alterations in human tissues, including reproductive organs. Exposure during development induces epigenetic alterations related to many diseases during adulthood, including infertility.
The aim of our study was to evaluate EDCs urine levels during early pregnancy and to correlate them with inflammatory activation of immune blood cells in both mothers and newborns.

Methods:
The patients included were enrolled in the perinatal medical service of the Instituto Nacional de Perinatología. All of them signed a letter of consent. Urine and blood samples were taken from mothers during pregnancy and blood samples from newborns at delivery. Concentrations of EDCs (phthalates and BPA) in urine were assessed by high-performance liquid chromatography coupled to mass spectrometry, and activation of immune blood cells from both mothers and newborns was assessed by flow cell cytometry.

Results:
Results showed urine levels of phthalate such as MEHP, DEHP and BPA higher than those recorded in similar populations worldwide, indicating that our population is exposed to high levels of these disruptors. In addition, phenotypic changes related to immune blood cell activation were observed in women with high levels of EDCs and their infants, compared to those mothers with lower levels. These findings indicate that maternal exposure to EDCs such as phthalates and BPA triggers activation of immune blood cells in mothers and newborns, resulting in alterations of physical properties and functional changes in immune blood cells, which may influence their ability to interact with other cells and tissues.

Conclusions:
These findings reveal the need for medical concern regarding human exposure to these compounds and promote strategies to reduce unintentional exposure to EDCs in order to prevent the impact on fetal programming and the development of diseases during adulthood.

Funding:
Financial support from PAPIIT, UNAM, IN201422., and PAIP 5000-9108, Facultad de Química, UNAM.

Key-words: (up to 5):

endocrine disruptors, fetal programming, pregnancy, immune blood cell activation, phthalates, BPA

Abstract #00005856 en

Association between pregestational nutritional status and neonatal outcomes in a chilean cohort.

Mechanisms Determining Transgenerational Effects of Health and Disease

Bertini Ayleen (1), Salas Rodrigo (2), Chiarello Delia Indira (1), Pardo Fabián (3)
(1) Escuela de Tecnología Médica, Facultad de Ciencias, Universidad San Sebastián, Santiago, Chile, (2) Escuela de Ingeniería Civil Biomédica, Universidad de Valparaíso, (3) Escuela de Medicina, Campus San Felipe, Universidad de Valparaíso

Background/aims:
Optimal maternal nutrition and nutritional status prior to pregnancy may play a critical role in reducing adverse neonatal outcomes. This study aimed to assess the association between pregestational nutritional status and multiple neonatal outcomes.

Methods:
A multicenter, cross-sectional descriptive study was conducted among pregnant women receiving primary healthcare services. Birth data were categorized according to pregestational nutritional status (underweight, normal weight, overweight, and obesity). Adverse neonatal outcomes evaluated included acute fetal distress (AFD), oligohydramnios (OHA), low birth weight (LBW), Apgar scores at 1 and 5 minutes, macrosomia, prematurity, and classifications of severely small, small, and large for gestational age (SSGA, SGA, LGA). A composite variable indicating the presence of one or more adverse outcomes was also analyzed. Associations were examined using the chi-square test, with statistical significance set at $p < 0.05$.

Results:
Statistically significant differences were observed between pregestational obesity and underweight groups in relation to adverse neonatal outcomes ($p = 0.002$). Pregestational obesity was significantly associated with an increased risk of macrosomia ($p < 0.001$) and LGA ($p < 0.001$), whereas pregestational underweight was associated with higher rates of LBW ($p = 0.002$), SGA, and SSGA ($p < 0.001$). No significant differences were found among the groups regarding AFD, OHA, Apgar scores, or prematurity.

Conclusions:
Pregestational nutritional status was significantly associated with specific adverse neonatal outcomes. Obesity prior to pregnancy increased risk of macrosomia and LGA, whereas underweight status was linked to a higher incidence of LBW, SGA, and SSGA. These results highlight the need to integrate nutritional evaluation and management into preconception and prenatal care strategies, aiming to reduce neonatal complications and improve birth outcomes.

Funding:
This research was supported by the Vicerrectoría de Investigación y Doctorados of Universidad San Sebastián. – Fondo USS – FIN. 25 – PDOC – 06, Fondo de Fomento al Desarrollo Científico y Tecnológico
(FONDEF)/XVIII Concurso Nacional de Proyectos de Investigación y Desarrollo en Salud, Fondo Nacional de Investigación y Desarrollo en Salud (FONIS)-7698SA21I009, Proyecto, UVA20993 y ANID Doctorado Nacional FOLIO 21231727

Key-words: (up to 5):

pregnancy, neonatal, nutritional state, nutrition in pregnancy

Abstract #00005857 en

Risk profile segmentation in chilean pregnant women using unsupervised Machine Learning: Application of DBSCAN for hidden pattern identification

Big Data and Cohorts in DOHaD Research.

Bertini Ayleen (1), Salas Rodrigo (2), Pardo Fabian (3), Chiarello Delia Indira (4)
(1) Universidad San Sebastián, (2) Escuela de Ingeniería Civil Biomédica, Universidad de Valparaíso, (3) Escuela de Medicina, Campus San Felipe, Universidad de Valparaíso, (4) Escuela de Tecnología Médica, Facultad de Ciencias, Universidad San Sebastián, Santiago, Chile

Background/aims:
Early identification of risk profiles during pregnancy is essential to prevent adverse outcomes. This study applied the unsupervised machine learning technique DBSCAN (Density-Based Spatial Clustering of Applications with Noise) to characterize groups of Chilean pregnant women based on sociodemographic and clinical factors.

Methods:
Data were analyzed considering maternal age, nationality, education level, occupation, pregestational obesity, diagnosis of gestational diabetes (GDM), hypertension (HTN), and intrauterine growth restriction (IUGR). DBSCAN identified six main clusters, including a noise group (-1).

Results:
DBSCAN analysis revealed six distinct clusters with differentiated sociodemographic and clinical characteristics. Cluster 2 grouped only younger pregnant women (100%) without pregestational obesity (100%), suggesting a low metabolic risk profile. Cluster 0 included a significant proportion of women with obesity (30.8%) and GDM (20.5%), while Cluster 3 showed higher prevalence of hypertension (15.6%), GDM (16.3%), and obesity (15.6%). Cluster 5 exhibited the highest rate of IUGR (25.0%), indicating a potential high neonatal risk profile. Regarding sociodemographic factors, clusters 0 and 1 mainly included women with medium educational levels (37.8% and 66.7%, respectively). Cluster 4 was characterized by all participants (100%) being homemakers.

Conclusions:
These findings highlight the existence of heterogeneous subgroups within the cohort that could benefit from tailored preventive interventions based on specific risk profiles. DBSCAN enabled the identification of hidden patterns linking sociodemographic and clinical factors in Chilean pregnant women. The results underscore the relevance of unsupervised machine learning techniques for risk segmentation in maternal health, supporting the development of more targeted interventions to improve maternal and neonatal outcomes.

Funding:
This research was supported by the Vicerrectoría de Investigación y Doctorados of Universidad San Sebastián. – Fondo USS – FIN. 25 – PDOC – 06, Fondo de Fomento al Desarrollo Científico y Tecnológico
(FONDEF)/XVIII Concurso Nacional de Proyectos de Investigación y Desarrollo en Salud, Fondo Nacional de Investigación y Desarrollo en Salud (FONIS)-7698SA21I009, Proyecto, UVA20993 y ANID Doctorado Nacional FOLIO 21231727

Key-words: (up to 5):

machine learning, artificial intelligence, bigdata, pregnancy

Abstract #00005859 en

Adherence to critical nutrient intake during pregnancy according to pre-gestational nutritional status in pregnant women attending public health centers in Chile.

Public Health Policies Across the Life Cycle.

Bertini Ayleen (1), Salas Rodrigo (2), Pardo Fabian (3), Chiarello Delia Indira (1)
(1) Escuela de Tecnología Médica, Facultad de Ciencias, Universidad San Sebastián, Santiago, Chile, (2) Escuela de Ingeniería Civil Biomédica, Universidad de Valparaíso, (3) Escuela de Medicina, Campus San Felipe, Universidad de Valparaíso

Background/aims:
Adequate intake of critical nutrients is fundamental for fetal development and maternal health. This study aimed to describe the adherence to critical nutrient intake according to nutritional status

Methods:
A multicenter, cross-sectional descriptive study was conducted in pregnant women attending primary healthcare services. The intake of critical nutrients (protein, folic acid, vitamin C, calcium, iron, and zinc) was assessed using two 24-hour recalls (R24H) administered on two non-consecutive days and categorized as insufficient, adequate, or excessive, according to the Dietary Reference Intakes. Pre-gestational nutritional status was classified according to BMI into underweight, normal weight, overweight, and obese. Cross-tabulations and the chi-square test were used, with post hoc analysis and Bonferroni correction, considering a p-value < 0.05 as significant.

Results:
A high prevalence of inadequate intake was observed for several nutrients. Inadequate folic acid intake was reported in 75% of women with normal weight, 74% overweight, and 73% obese. Vitamin C intake was insufficient in 50% of the normal and overweight groups and 52% of the obese group. Iron intake was insufficient in nearly all participants (100% of normal weight and overweight, 95% of obese). Calcium intake inadequacy increased with BMI (81% in normal weight, 85% overweight, 93% obese), with a significant difference between the obese and normal weight groups ($p = 0.024$). Protein intake was generally adequate across BMI categories. Zinc intake showed notable insufficiency, particularly in the normal weight group (69%).

Conclusions:
The distribution of adequate nutrient intake varied across pre-gestational BMI categories, suggesting potential differential nutritional risks based on maternal weight status. These findings underscore the need for targeted nutritional interventions to improve the dietary intake of pregnant women and ensure optimal maternal and fetal health, in addition to the longitudinal characterization of the diet in pregnant women with different nutritional statuses.

Funding:
This research was supported by the Vicerrectoría de Investigación y Doctorados of Universidad San Sebastián. – Fondo USS – FIN. 25 – PDOC – 06, Fondo de Fomento al Desarrollo Científico y Tecnológico
(FONDEF)/XVIII Concurso Nacional de Proyectos de Investigación y Desarrollo en Salud, Fondo Nacional de Investigación y Desarrollo en Salud (FONIS)-7698SA21I009, Proyecto, UVA20993 y ANID Doctorado Nacional FOLIO 21231727

Key-words: (up to 5):

nutrition, nutrition in pregnancy, pregnancy

Abstract #00005860 en

Gestational and lactational exposure to plastic waste induces inflammation and oxidative imbalance in the prostate of adult rats

Impact of Early Life Exposures and Environmental Pollutants

Aguiar Rocha Vanessa (1), Vieira de Souza Patrick (1), Magosso Natália (1), Cavalheiro Marina (1), Cristina Pinha Victória (1), Franco Moreira Mirella (1), Hipolito Quadreli Debora (2), Scantamburlo Alves Fernandes Glaura (2), Rodrigo Scarano Wellerson (1)
(1) Institute of Biosciences, São Paulo State University (UNESP), Botucatu, São Paulo, Brazil, (2) Biological Sciences Center, State University of Londrina, Londrina, Paraná, Brazil

Background/aims:
The intrauterine microenvironment is susceptible to alterations caused by environmental factors, which can result in long-term consequences for the offspring. Given the ability of plastic waste to cross the placental barrier and to act as endocrine disrupting chemicals, this study aims to evaluate the effects of perinatal exposure to an environmentally relevant phthalate mixture (PM) and nanoplastics (NPs) on the prostate of adult rats.

Methods:
Pregnant Sprague-Dawley rats were assigned to six experimental groups: control (vehicle), T1 (20µg MP), T2 (200mg MP), T3 (NPs), T4 (20µg MP + NPs), T5 (200mg MP + NPs). The treatment was administered orally from gestational day 10 to postnatal day (PND) 21. The pups were euthanized at PND120, and the ventral prostate was collected (Ethical protocol nº1174020523). The ANOVA test was used (P≤0.05).

Results:
Histological analysis showed an increase in the inflammatory foci incidence and stromal compartment in the prostate of animals exposed (T1, T2, T3, T4 e T5), and a decrease in the luminal compartment in T1, T3, T4 groups compared to the control. An increase in total and degranulated mast cells was observed, as well as an increase in immunoreactivity pattern for androgen receptor in all exposed groups compared to the control. All exposed groups showed an increase in Tnf-α expression. Analysis of the oxidative profile showed an increase in lipid peroxidation and glutathione S-Transferase activity in all treated groups, a decrease in the catalase activity in the T1, T3, T5 groups, as well as an increase in the superoxide dismutase in the T3, T4, T5 groups and an increase in glutathione (GSH, GSSG, GT) in the G5 compared to the control.

Conclusions:
These findings suggest that the treatment was able to induce significant damage to the prostate, triggering inflammatory processes and oxidative imbalance that may influence the pathogenesis of adaptive or neoplastic disorders.

Funding:
State of São Paulo Research Foundation (FAPESP, Grant 2023/12506-8)

Key-words: (up to 5):
Histology. Nanoplastics. Phthalates. Prostate.

Abstract #00005877 en

Maternal Exposure to High-Sucrose Diet Deteriorates the Offspring Periovarian Microenvironment

Impact of Early Life Exposures and Environmental Pollutants

Champoudry da Silva O (1), Soares JF (1), França LM (1), Brito CFC (1), Paes AMA (1) (1) Federal University of Maranhão, São Luís, (MA), Brazil

Background/aims:
Maternal nutrition is critical to offspring metabolic and reproductive health. Obesogenic diets have been shown to impair the periovarian adipose tissue (POAT), which plays a main role on gonads microenvironment. However, the impact of maternal high-sucrose intake, a current concern in Latin America, remains poorly understood. Thus, this study aimed to assess the impact of maternal high-sucrose consumption on the female offspring's morphophysiological profile of POAT and gonads.

Methods:
Female Wistar rats were fed a regular chow (CTR, 10% sucrose, n = 6) or high-sucrose diet (HSD, 25% sucrose, n = 6) 6 weeks prior and throughout gestation and lactation. Offspring was fed regular chow from weaning up to 120 days-old, when for morpho-functional assessments of POAT and ovaries were performed. Yet, the onset of puberty and estrous cyclicity at adulthood were monitored (23115.038755/2018-22 CEUA/UFMA).

Results:
HSD mothers showed increased pre-gestational body mass (Lee Index: 318.0±1.2 vs 328.2±2.0 g, $p<0.05$), which associated with the increase of offspring body weight at birth (5.92±0.05 vs 6.18±0.07 g, $p<0.05$) and weaning (49.54±0.73 vs 53.83±0.88 g, $p<0.05$). Perinatal exposure to HSD did not affect the time of menarche or estrous cyclicity, but slightly increased the number of atretic follicles at 120 days-old. On the other hand, HSD offspring showed POAT adipocyte hypertrophy (1,975.00±34.35 vs 2,857.00±62.01 µm2, $p<0.05$). Additionally, ex-vivo POAT lipolytic response to isoproterenol was not affected, but antilipolytic response to insulin was impaired.

Conclusions:
Maternal HSD intake induces POAT hypertrophy and decreases its sensitivity to insulin, which may contribute to ovarian deterioration characterized by follicular atresia. These findings highlight the importance of healthy maternal nutrition in shaping offspring reproductive and metabolic health.

Funding:
CNPQ, CAPEs, and FAPEMA

Key-words: (up to 5):
Added sugars, Fetal Programming, Reproductive Health

Abstract #00005905 en

Violência Interpessoal: análise das notificações do SINAN referentes a um município de Pernambuco

Public Health Policies Across the Life Cycle.

Santana Costa Carvalho Rebecka (1), Newman Leite dos Santos Lucena Renata (2), Santana da Silva Karl Marx (1) (1) Universidade Federal de Pernambuco, (2) Universidade Federal da Paraíba

Background/aims:
O conceito das Origens Desenvolvimentistas da Saúde e da Doença (DOHaD) postula que exposições ambientais adversas desde a concepção até os primeiros anos de vida, podem alterar a trajetória do desenvolvimento. Essas exposições incluem fatores como o estresse tóxico, entre os quais temos a violência interpessoal, representando um fator estressor significativo na infância. O presente estudo busca analisar os dados de violência interpessoal de um município de Pernambuco que carece de estudos e informações sobre os diversos agravos que atingem sua população.

Methods:
Trata-se de um estudo descritivo, transversal e retrospectivo dos casos de violência interpessoal referentes a um município da região metropolitana de Recife-PE de 2011 a 2020.

Results:
Durante o período de 2011 a 2020 foram notificadas um total de 9.782 casos de violência interpessoal no município. Em relação as vítimas 68,2% sexo feminino, 63,5% pardas, 32,1% solteiros e 39,6% heterossexual; residência das vítimas foi o local de maior frequência para os casos de agressão, 56%; violência física apresentou maior percentual, 52,7%, seguido pela negligência/abandono, 17,3% e a violência psicológica, 12,1%; com respeito aos meios de agressão força corporal/espancamento 37,6% dos casos, envenenamento/intoxicação em 18,3%; quanto às informações do possível agressor da violência 60,9% sexo masculino, 30,3% envolviam dois ou mais indivíduos e 33,6% tinham de 25 a 59 anos; sobre o vínculo de parentesco encontramos o cônjuge, 12,8%, autor desconhecido/desconhecido, 11,1%, mãe 9% e ex-cônjuge 7,2%.

Conclusions:
O presente trabalho foi capaz de agregar conhecimento a respeito da violência interpessoal e apresentar a sociedade padrões em relação às vítimas, os agressores e as violências que são mais prevalentes e utilizar como subsídio para estabelecer intervenções e se trazer um feedback, quantitativo, em relação ao desempenho das políticas públicas de enfrentamento e combate à violência interpessoal neste município.

Funding:
Este estudo não contou com financiamento externo, sendo inteiramente custeado pela pesquisadora

Key-words: (up to 5):
Violência interpessoal, Prevalência, Notificação,DOHaD

Abstract #00005913 en

Prevalence of overweight in preschoolers from schools linked to the Health in Schools Program in Southern Brazil

Public Health Policies Across the Life Cycle.

Mallmann Lessa Samantha (1), Rombaldi Bernardi Juliana (2), Ramos Magalhães Cleidilene (3), Cardoso Tietzmann Daniela (3), Silva dos Santos Francine (3)
(1) Universidade Federal do Rio Grande do Sul _UFRGS, (2) Universidade Federal do Rio Grande do Sul _ UFRGS, (3) Universidade Federal de Ciências da Saúde de Porto Alegre - UFCSPA

Background/aims:
Childhood obesity is a chronic multifactorial disease, on the rise globally, and represents a risk factor for several chronic non-communicable diseases. Early prevention is especially relevant in low- and middle-income countries. Influential factors include genetic, behavioral, environmental and political aspects. In this context, the Health in School Program (PSE) stands out, which integrates Primary Health Care actions with the school environment with a focus on promotion and prevention. This study aimed to verify the prevalence of overweight in preschoolers from schools that are part of the PSE and those that are not part of the PSE in the city of Guaíba, Rio Grande do Sul.

Methods:
This is a retrospective cross-sectional study carried out with 345 preschoolers, from levels 1 and 2 (4 to 6 years old) of Municipal Early Childhood Education Schools (EMEIs), which include 10 school units, distributed in four regions that encompass the majority of the territory of the municipality of Guaíba, with 7 school units agreed upon in the PSE and 3 not agreed upon in this program of the Brazilian federal government.

Results:
The data indicate that preschoolers attending schools that are part of the PSE are less likely to develop excess weight. In the multivariate logistic regression model, adjusted for sex and region, the data analyzed in this population suggest that the Health in School Program (PSE) may reduce the chances of preschoolers developing excess weight.

Conclusions:
The PSE shows promise in preventing overweight in preschoolers, reinforcing the importance of intersectoral public policies between health and education. Promoting healthy school environments can significantly contribute to better habits and child well-being. Follow-up studies will be needed to monitor these effects over time.

Funding:
Unfunded research.

Key-words: (up to 5):
Childhood Obesity. Food and Nutrition Education. Health Promotion at School. Early Childhood Education.

Abstract #00005916 en

Interpersonal Violence: analysis of SINAN notifications related to a municipality in Pernambuco

Public Health Policies Across the Life Cycle.

Santana Costa Carvalho Rebecka (1), Newman Leite dos Santos Lucena Renata (2), Santana da Silva Karl Marx (1) (1) Universidade Federal de Pernambuco, (2) Universidade Federal da Paraíba

Background/aims:
The concept of Developmental Origins of Health and Disease (DOHaD) posits that adverse environmental exposures from conception to early life can alter the trajectory of development. These exposures include factors such as toxic stress, including interpersonal violence, which represents a significant stressor in childhood. This study seeks to analyze data on interpersonal violence in a municipality in Pernambuco that lacks studies and information on the various problems that affect its population.

Methods:
This is a descriptive, cross-sectional and retrospective study of cases of interpersonal violence in a municipality in the metropolitan region of Recife-PE from 2011 to 2020.

Results:
During the period from 2011 to 2020, a total of 9,782 cases of interpersonal violence were reported in the municipality. Regarding the victims, 68.2% were female, 63.5% were mixed race, 32.1% were single, and 39.6% were heterosexual; the victims' residence was the most frequent location for cases of aggression, 56%; physical violence had the highest percentage, 52.7%, followed by neglect/abandonment, 17.3%, and psychological violence, 12.1%; with respect to the means of aggression, physical force/beating in 37.6% of the cases, poisoning/intoxication in 18.3%; regarding the information on the possible aggressor of the violence, 60.9% were male, 30.3% involved two or more individuals, and 33.6% were between 25 and 59 years old; regarding the family relationship we found the spouse, 12.8%, unknown/unknown author,
11.1%, mother 9% and ex-spouse 7.2%.

Conclusions:
This work was able to aggregate knowledge regarding interpersonal violence and present society with patterns in relation to victims, aggressors and the most prevalent types of violence and use them as a subsidy to establish interventions and provide quantitative feedback regarding the performance of public policies to confront and combat interpersonal violence in this municipality.

Funding:
This study did not receive external funding and was entirely funded by the researcher

Key-words: (up to 5):
Violence, Prevalence, Notification, DOHaD

Abstract #00005917 en

Exploring the Role of Western Dietary Pattern and Nutritional Status as Mediators of Gestational Diabetes Risk in a Prospective Study

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Lambert Victoria (1), Muñoz Sonia Edith (2), Osella Alberto Ruben (3), Miranda Virginia Soledad (3), Wirtz Baker Julia Mariel (1), Aballay Laura Rosana (3), Román María Dolores (3)
(1) INICSA (CONICET-UNC); CENINH (EN-FCM-UNC), (2) INICSA (CONICET-UNC), (3) CENINH (EN-FCM-UNC)

Background/aims:
Gestational diabetes mellitus (GDM) affects the health of women and their offspring, as a result of a complex interaction of nutritional, lifestyle and contextual factors. We estimated the effect of Western pre-pregnancy dietary pattern on GDM, examining the role of this pattern during pregnancy and body mass index (BMI) as mediating pathways in pregnant women from Cordoba (Argentina).

Methods:
A prospective observational study was conducted (n=239). Dietary intake was assessed using a food frequency questionnaire. Principal components factorial analysis was applied to identify pre-pregnancy and pregnancy dietary pattern. BMI, lifestyle and contextual factors were also evaluated. The diagnosis of GDM was recorded. A generalised structural equation model was performed to examine mediating effects of Western pregnancy dietary pattern and BMI on the Western pre-pregnancy dietary pattern-GDM relationship, adjusting for age, gestational weight gain, parity, socioeconomic status, physical activity and smoking (Stata v17). All procedures adhered to ethical healthcare guidelines. (REPIS n°004).

Results:
GDM incidence was 7.11% (95% CI: 4.19%; 11.14%). Western dietary patterns -characterised by intake of refined cereals, processed meats, sweet drinks, cheese and fatty foods- were identified in pre-pregnancy and pregnancy periods. Non-association (direct effect) was observed between Western pre-pregnancy dietary pattern and GDM (β=-0.96 95%CI: -2.22; 0.28). A higher adherence to Western pre-pregnancy dietary pattern was positively associated with higher adherence to Western pregnancy dietary pattern (β=0.25, 95%CI: 0.13; 0.37) and negatively associated with a one-unit increase in BMI (β=-1.34, 95%CI: -2.62; -0.60). A higher adherence to Western pregnancy dietary pattern (β=1.72, 95%CI 0.38; 3.12) and an increase in BMI (β=0.12, 95%CI: 0.02; 0.23) was positively associated with GDM.

Conclusions:
A higher adherence to a Western pre-pregnancy dietary pattern indirectly contributed to an increase in GDM risk through the pathways of Western pregnancy dietary pattern and BMI, reinforcing the need for early nutritional intervention during prenatal care.

Funding:
CONICET fellowship; FONCYT grant PICT-2020/03283; SECyT-UNC grant 258/23.

Key-words: (up to 5):
Gestational Diabetes Mellitus; Dietary Pattern; Body Mass Index; Mediating Effects; Maternal and Child Health

Abstract #00005956 en

High-Fat Diet Consumption by Female Rat Offspring of Obese Mothers Exacerbates Adipose Tissue Expansion and Metabolic Dysfunction in Adult Life

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Rodríguez-González Guadalupe L. (1), Reyes-Castro Luis A. (1), Prieto-Ibañez Vidblain (1), Ibáñez Carlos A. (1), Juárez-Pilares Gimena (2), Zambrano Elena (3)

(1) Biología de la Reproducción, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, (2) DIEB, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, (3) Biol Reproducción, Instituto Nacional de Ciencias Médicas y Nutrición SZ/Facultad de Química, UNAM

Background/aims:

Maternal obesity (MO) increases offspring obesity risk. Unhealthy postnatal dietary habits also promote obesity. Therefore, it is important to evaluate whether offspring who follow their mothers' bad dietary patterns are more likely to become obese. We aimed to determine whether postnatal consumption of a high-fat diet (HFD) exacerbates body fat accumulation and metabolic changes in the female offspring of obese mothers.

Methods:

Female Wistar rats ate chow (C: 5%-fat) or HFD (MO: 25%-fat) from weaning through pregnancy and lactation. Female F1 were weaned on chow or HFD (second hit C/HF and MO/HF). At 110 days, body weight was recorded, F1 were euthanized and fat depots were removed to estimate adiposity index (AI). Serum glucose, triglycerides by colorimetry, insulin, corticosterone, and dehydroepiandrosterone (DHEA) by ELISA. Insulin resistance index (HOMA-IR) was determined. Adipocyte size distribution in retroperitoneal fat was modeled by gamma distribution. Procedures followed institutional ethical guidelines. C/C, C/HF and MO/HF (n=8) and C/MO (n=7). Analysis by two-way ANOVA.

Results:

C/HF and MO/HF exhibited greater body fat accumulation and AI than C/C and MO/C. MO/HF showed the highest HOMA-IR compared to MO/C and C/HF. Triglycerides and corticosterone were higher in C/HF and MO/C than in C/C, and exacerbated in MO/HF vs. C/HF. DHEA concentrations and the DHEA/corticosterone ratio were lower in C/HF and MO/C than in C/C, but higher than in MO/HF. No differences were observed in glucose and insulin concentrations, or small adipocytes. Large adipocytes increased in C/HF and were exacerbated in MO/HF.

Conclusions:

Female F1 metabolic disorders are caused by MO or suboptimal dietary habits. However, the combination of developmental programming by MO and postnatal exposure to a HFD (second hit) worsens the metabolic dysfunction by exacerbating corticosterone concentrations (key regulator) and increasing the large adipocytes.

Funding:

FONCICYT/49/2016.

Key-words: (up to 5):

Maternal obesity, high-fat diet, metabolic alterations, adipose tissue.

Abstract #00005958 en

Gestational weight gain trajectories associated with birth outcomes: results from the Brazilian maternal and child nutrition consortium

Big Data and Cohorts in DOHaD Research.

Nigri Cursino Giovana (1), Sousa José Thiago Alves (1), Oliveira Nathália Teixeira (1), Kac Gilberto (1), Farias Dayana Rodrigues (1), Consortium Gestational Weight Gain (2)
(1) Federal University of Rio de Janeiro, (2) Nutrition Epidemiology Observatory

Background/aims:
Gestational weight gain (GWG) above or below the recommended levels is associated with a variety of adverse effects on maternal and fetal outcomes, including changes in birth weight. This study aimed to identify the trajectories of GWG and evaluate the association with low birth weight (LBW) and macrosomia.

Methods:
Data from ten cohorts conducted in Brazil between 1990-2018 were used. Women aged 18-45 were included, and pre-pregnancy weight (kg), height (cm), pre-pregnancy BMI (kg/m2), GWG (the difference between the weight measured at the last prenatal visit and the weight at conception; kg) and gestational age (weeks) were measured. LBW (< 2500g) and macrosomia (≥ 4000g) were the birth outcomes. The GWG trajectories were identified using the latent class growth model, and their association with the birth outcomes was estimated using a logistic regression model adjusted for maternal age, pre-pregnancy BMI, smoking status and gestational age. Approved by the ethics committee of UFRJ (CAAE: 33897420.4.0000.5275).

Results:
A total of 15,338 women and 88,142 observations were included in the analysis. We identified five GWG trajectories: 1)“Stable-low” (8.1%;n=1,239) with low GWG throughout the entire pregnancy; 2)“Stable-medium” (31.6%;n=4,849) with medium gain (reference in the model); 3)“High” (19.8%;n=3,032) with pronounced GWG as in the second trimester; 4)“Medium-High” (35.1%; n=5,383) with high and more pronounced gains from the third trimester; 5)“Earlier-high” (5.4%; n=835) with rapid and high gains from the beginning of pregnancy. The prevalence of LBW was 5.2% and of macrosomia 8.5%. Women in the “Stable-low” trajectory (OR=1.31;95%CI:1.14–1.51) had higher odds of having infants with LBW. At the same time, women in the trajectories “High” (OR=1.86; 95%CI:1.68–2.05), “Medium-High” (OR=1.29;95%CI:1.17-1.41) and “Earlier-High” (OR=3.70;95%CI:3.25–4.21) had higher odds of having babies with macrosomia.

Conclusions:
The results contribute to the understanding of GWG trajectories and their relationship with neonatal outcomes, highlighting the need to support prenatal nutrition interventions in primary health care.

Funding:
Coordination for the Improvement of Higher Education Personnel – CAPES.

Key-words: (up to 5):
Gestational weight gain trajectory, Excess weight gain, Inadequate weight gain, Low birth weight,

Macrosomia

Abstract #00005964 en

Machine Learning Models for Predicting Failure of Postnatal Weight Catch-Up in the First 1,000 Days: Evidence from the BRISA Birth Cohort

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Jardim Ana Tamires (1), de Souza Bruno Feres (1), Ferreira Cibelly de Fátima Vieira (1), Viola Poliana Cristina de Almeida Fonseca (1), Thomaz Erika Barbara Abreu Fonseca (1)
(1) Programa de Pós-Graduação em Saúde Coletiva. Universidade Federal do Maranhão – UFMA, Brasil

Background/aims:
Postnatal weight catch-up, a phase of accelerated growth following intrauterine or early life growth restriction, plays a critical role in mitigating long-term adverse health outcomes. The inability to achieve adequate catch-up growth is associated with increased risk of morbidity and impaired developmental trajectories. This study aimed to develop and evaluate predictive models using machine learning algorithms to identify children at heightened risk of failing to attain weight catch-up within the first 1,000 days of life.

Methods:
We analyzed a subsample of 401 children under 25 months of age born with low or very low weight-for-age, drawn from the Ribeirão Preto and São Luís birth cohorts (BRISA). Eleven maternal and child variables spanning intergenerational, sociodemographic, perinatal, and clinical domains were included as predictors: maternal age, occupation, skin color, cohabitation with a partner, child head circumference, history of hospitalization, prematurity, prenatal care characteristics, smoking during pregnancy, and number of previous children. The primary outcome was defined as a ≤0.67 increase in weight-for-age z-score by 24 months, indicating failure to achieve catch-up growth.

Results:
Predictive models were developed using six machine learning algorithms: Random Forest, Logistic Regression, XGBoost, Support Vector Machine, and Decision Tree. Model performance was evaluated using standard classification metrics, including accuracy, precision, recall (sensitivity), specificity, F1-score, and the area under the receiver operating characteristic curve (AUC-ROC). Among all models tested, Random Forest demonstrated the most robust performance, achieving an accuracy of 0.70, F1-score of 0.71, sensitivity of 0.82, specificity of 0.58, and an AUC-ROC of 0.74.

Conclusions:
Our findings demonstrate that machine learning models, particularly Random Forest, are effective in predicting failure to achieve weight catch-up ,to accurately identify children at risk of suboptimal postnatal growth. Such predictive tools may support early clinical decision-making and targeted interventions to promote optimal health trajectories during this critical developmental window.

Funding:
Support received from the Brazilian National Council for Scientific and Technological Development (CNPq) **Key-words: (up to 5):**

machine learning , children; health

Abstract #00005970 en

Disruptions in the placental serotoninergic system are associated with impaired neurodevelopment in one-month old infants

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Canul-Euan Arturo Alejandro (1), Flores-Pliego Arturo (2), Espejel-Nuñez Aurora (2), Parra-Hernandez Sandra (2), Solis-Paredes Juan Mario (2), Mendoza-Hernández Tahiri (2), Gil-Martinez Gabriela (2), Hernandez-Chavez Maria del Carmen (2), Camacho-Arroyo Ignacio (3), Estrada-Gutierrez Guadalupe (2)
(1) Instituto Nacional de Pediatria / Star Medica Hospital Infantil Privado, (2) Instituto Nacional de Perinatología Isidro Espinosa de los Reyes, (3) Instituto Nacional de Perinatología Isidro Espinosa de los Reyes / Facultad de Química, UNAM

Background/aims:
Serotonin (5-HT) plays a critical role in numerous physiological processes, including brain development. However, the contribution of the placental serotoninergic system to early neurodevelopmental outcomes remains underexplored. This study aims to evaluate the association between components of the placental serotonergic system and neurodevelopment in infants during the first month of life.

Methods:
This study was approved by the IRB of the National Institute of Perinatology (INPer) in Mexico City (2021-1-11) and included 49 participants from the OBESO cohort (3300-11402-01-575-17; 2024-1-14). Infant neurodevelopment was assessed at one month using the Bayley Scales of Infant Development, Third Edition (BSID-III); scores ≤7 in any domain were considered altered. Placental 5-HT was measured by ELISA and correlated with neurodevelopmental scores. A subset of placental samples (normal vs altered neurodevelopment) was analyzed by Western blot to quantify the expression of the 5-HT-related proteins, including tryptophan hydroxilases (TPH1 and TPH2), the serotonin transporter (SERT), the monoamine oxidase A (MAO-A), and the receptors 5HT1E and 5HTR5.

Results:
Placentas from infants with altered neurodevelopment showed increased expression of TPH1, TPH2, and SERT, and significantly reduced levels of MAO-A. Additionally, placental 5-HT concentrations were elevated in infants with low language composite scores.

Conclusions:
Dysregulation of the placental serotonergic system is associated with impaired neurodevelopment during the first month of life. These findings suggest that placental serotonin signaling may play a role in early brain programming and could contribute to later-life mental health disorders.

Funding:
Instituto Nacional de Perinatología Isidro Espinosa de los Reyes (Grants 2021-01-11 to I.C.-A; 3300-11402-01-575-17 to G.E-G.)

Key-words: (up to 5):
neurodevelopment, serotonin, infant, human, placenta

Abstract #00005975 en

Maternal High-Fat and High-Sucrose Diets Differentially Alter Memory Behavior and Hippocampal Transcriptome in Offspring

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Baqueiro Mayara (1), Costa Suleyma Oliveira (1), Nascimento Luciana C. P. (1), Campos Aline Franco (1), Torsoni Marcio Alberto (1), Ross Michael Gleen (2), Desai Mina (3), Torsoni Adriana Souza (1)
(1) School of Applied Sciences, University of Campinas (UNICAMP), (2) The Lundquist Institute at Harbor-UCLA Medical Center, (3) The Lundquist Institute at Harbor-UCLA Medical Center, UCLA

Background/aims:
Maternal consumption of a Western Diet, characterized by high levels of saturated fats and sucrose, during pregnancy and lactation can negatively affect metabolic outcomes in offspring. This dietary pattern is link to metabolic disorders that trigger neuroinflammation and impair cognition function. This study aimed to evaluate the effects of maternal high-sucrose or high-fat diet on the memory behavior and hippocampal CA3 transcriptome of offspring, a critical area for learning and associative memory.

Methods:
Female mice were fed a control diet (CT 10% fat, 7% sucrose, n=6-9), a high sucrose diet (HS 10% fat, 35% sucrose, n=13-18), or high-fat diet (HF 45% fat, 17% sucrose, n=5-6) prior to and during pregnancy and lactation. After birth, the offspring were weaned onto CT. At 12 weeks, the Novel Object Recognition (NOR) test was performed to assess memory. Following testing, offspring were euthanized and the hippocampal CA3 area was sampled for RNA sequencing (transcriptome analysis).

Results:
Female offspring of HS dams exhibited shorter exploration time (p=0.034) and a lower discrimination ratio for the novel object (p=0.044) compared to those from CT dams, while no differences were observed in the offspring of female HF dams compared to CT. In contrast, male offspring of HF dams showed a lower discrimination ratio for the novel object compared to both CT (p=0.05) and HS (p=0.017) groups. Transcriptome analyses of the CA3 region revealed that HS female offspring exhibited upregulation of TERT1 and CXCR4 genes (2.0FC), which are involved in stem cell proliferation and cytokine response. Meanwhile, HF male offspring displayed upregulation of POMC and MC4R genes (2.5FC) which may play a role in the integration of stress responses and energy homeostasis.

Conclusions:
These findings suggest that exposure to HS or HF during development can have distinct and detrimental effects on behavior and memory in both female and male offspring.

Funding:
NIH grant #R01HD099813.

Key-words: (up to 5):
High-Fat-Diet, High-Sucrose-Diet, Metabolic-Programming, Hippocampus, Offspring

Abstract #00006004 en

Prenatal and early life factors on predicting Allergic Traits at 2 years of age: a machine learning approach

Big Data and Cohorts in DOHaD Research.

Sá Rafaela Vitória Pereira (1), Viola Poliana Cristina Fonseca (1), Alves-Costa Silas (1), Feres Bruno (1), Ribeiro Cecilia Claudia Costa (1)
(1) Universidade Federal do Maranhão

Background/aims:
Dermatitis, rhinitis, and food allergies are interconnected conditions that form part of the "atopic march", which involves allergy-mediators such as eosinophils. As a result, in addition to immunnological pathways, these conditions may share overlapping risk factors. This study employs machine learning algorithms to assess the predictive accuracy of diagnosing Allergic Traits in the second year of life, using a set of prenatal and early postnatal predictors.

Methods:
Data from the BRISA prenatal cohort in São Luís, Brazil, were utilized with complete outcome information of 1158 mothers and their offspring. Allergic traits were defined as the presence of a medical diagnosis of dermatitis, rhinitis, food allergies, or eosinophil counts ≥300 in the second year of life. Predictors included pregnancy conditions and child information up to 6 months of age, chosen based on literature/expert input. Machine learning techniques were applied, and feature interpretation was made using SHapley Additive ExPlanations (SHAP) regarding the outcome. All participants gave written consent (Ethics Committee #4771/2008-30).

Results:
In the sample, 53.5% of children exhibited allergic traits. A model using the SVM Linear algorithm achieved 55.3% (CI95% 52.4; 58.2%) accuracy, 50.9% sensitivity, and 60.4% specificity. A family history of dermatitis, rhinitis, or asthma was the main feature contributing to the outcome, followed by early introduction of foods, low-income families, high frequency of soft drink consumption, hypertension during pregnancy, and higher maternal age. Gestational diabetes and alcohol consumption contributed the least to the model.

Conclusions:
Overall, our model exhibited moderate predictive accuracy in identifying allergic traits at age of two. These findings suggest that genetic factors play an important role in the development of allergic diseases. They also highlight the relevance of maternal factors, such as unhealthy habits and pre-existing chronic conditions, as key targets for early prevention. Additionally, the results emphasize the significance of appropriate food introduction in reducing allergy risks.

Funding:
This work was supported by the Brazilian Ministry of Health/DECIT/CNPq [no. 400759/2024-1] in partnership with the Gates Foundation.

Key-words: (up to 5):
Machine Learning; Allergy; Prenatal Care

Abstract #00006006 en

Process of co-creating an Aboriginal and Torres Strait Islander longitudinal pregnancy cohort study: The Strong Families Study

Big Data and Cohorts in DOHaD Research.

Rae Kym (1), Massi Luciana (2), Smith Davina (2), Ahmed Salma (2), Weatherall Loretta (2), Friday Rhiannon (2), Dorey Emily (2), Wheeler Kai (2), Indigenous Steering Committee Strong Families Study (2)
(1) Mater Research Institute - University of Queensland, (2) Indigenous Health Research group, Mater Research Institute, QLD Australia

Background/aims:
The Strong Families Study is a groundbreaking Indigenous-led research project to support Aboriginal and Torres Strait Islander families during the First 1000 days, emphasising the voices and lived-experiences of Indigenous peoples. Central to its success was the co-creation approach, ensuring Indigenous leadership and culturally responsive methodologies were embedded.

Methods:
A co-creation approach was undertaken in partnership with an Indigenous Steering Committee (ISC) with members from over 16 Indigenous health services in Queensland, providing leadership, Indigenous knowledge, experiences, and priorities. Co-creation workshops applied the Aboriginal practice of Dadirri, that is inner deep listening and quiet still awareness, and yarning, which facilitated deep connections and helped re-dress power imbalances between researchers and ISC members. Other strategies effectively incorporated sticker exercises, active discussions and reaching consensus across the group.

Results:
The key outcome of this co-creation process included the development of culturally responsive health priorities, informed consent practices, data collection and governance processes. The group prioritised self-determination and fostered ongoing meaningful dialogue between researchers and community members, reinforcing the study's ethical and culturally responsive approach.

Conclusions:
The Indigenous practices of Dadirri and yarning were instrumental in guiding the co-creation process, ensuring Indigenous voices were valued and prioritised in the research, enhancing the cultural integrity of the study. The transformative impact of the research process was stated by ISC members following the co-creation workshops. This presentation will share processes and the protocol developed for the Strong Families Study. These serve as a model for Indigenous-led research, demonstrating the significant role of Indigenous leadership and knowledge in shaping health research and outcomes.

Funding:
This study was funded by the National Health and Medical Research Council (NHMRC GNT2023832), as part of the Strong Families Cohort study funded through the Clinical Trials and Cohort Scheme.

Key-words: (up to 5):
Indigenous Peoples, Australian Aboriginal and Torres Strait Islander Peoples, birth cohort study, longitudinal study, culturally sensitive care, shared decision making, community-based participatory research.

Abstract #00006007 en

Using Supervised Machine Learning to Predict Asthma Traits at the 2nd year: Analyzing Pregnancy and Early-Life Conditions

Big Data and Cohorts in DOHaD Research.

Sá Rafaela Vitória Pereira (1), Viola Poliana Cristina Fonseca (1), Alves-Costa Silas (1), Feres Bruno (1), Ribeiro Cecilia Claudia Costa (1)
(1) Universidade Federal do Maranhão

Background/aims:
Asthma is the most common non-communicable disease among children. The etiology of asthma is not yet fully understood; it may start in early-life. The present study aims to assess predictive accuracy of factors related to asthma traits at 2 years of age, focusing on prenatal and early postnatal factors.

Methods:
The research evaluated a total of 1151 mother-child pairs from the BRISA prenatal cohort, São Luís, Brazil, with data on the outcome. Asthma traits were defined either by a medical diagnosis or wheezing episodes at the age of two. The authors independently selected a set of predictors based on previous literature. Machine learning techniques were evaluated, and SHAPley Additive exPlanations (SHAP) were used to interpret the contribution of each predictor to the outcome. All participants provided written consent (Ethics Committee #4771/2008-30).

Results:
The prevalence of asthma traits was found to be 30.6%. The Support Vector Machine algorithm achieved an accuracy of 58.6%(CI95% 55.7;61.5), 51.8% sensitivity, 61.8% specificity, and 0.43 F1 score. SHAP analysis identified five main predictors for the development of asthma traits at the age of 2: weekly consumption of soft drinks and ice cream during pregnancy, belonging to a low-income family, family history of asthma, dermatitis or rhinitis, and gestational hypertension. Other significant factors included a lower number of prenatal appointments, alcohol consumption during pregnancy, periodontitis, being multiparous, vaginal discharge and, early food introduction. Notably, older maternal age during pregnancy was associated with a lower risk of developing asthma traits. Depression, measured by CESD scale, was not an effective discriminator for the outcome.

Conclusions:
Our model demonstrated moderate predictive accuracy for asthma traits at two years of age. Behavioral risk factors, family history, and maternal health conditions emerged as the main predictors. This highlights the importance of interventions targeting early-life events to help prevent the onset of non-communicable diseases in childhood.

Funding:
This work was supported by the Brazilian Ministry of Health/DECIT/CNPq[no.400759/2024-1] in partnership with the Gates Foundation.

Key-words: (up to 5):
Machine learning; Childhood asthma; Prenatal care

Abstract #00006009 en

Interactions Between Prenatal Fluoride Exposure and Neurotransmission-Related Gene Variants on Child Neurodevelopment in a Mexican Prospective Cohort

Impact of Early Life Exposures and Environmental Pollutants

Santiago Ángel (1), Bashash Morteza (2), Garza Mayra J (1), Martínez-Mier Esperanza Ángeles (3), Hu Howard (2), Peterson Karen E (4), Téllez-Rojo Martha M (5), Lamadrid-Figueroa Hector (1)
(1) Departamento de Salud Perinatal, Instituto Nacional de Salud Pública de México, (2) Keck School of Medicine, University of Southern California, (3) School of Dentistry, Indiana University, (4) School of Public Health, University of Michigan, (5) Center for Nutrition and Health Research, National Institute of Public Health

Background/aims:
Based on systematic review, the US National Toxicology Program recently concluded that higher early life fluoride exposure is consistently associated with adverse neurodevelopmental effects. We investigated whether single nucleotide polymorphisms (SNPs) in neurotransmission-related genes modify the association between prenatal fluoride exposure on children's cognitive and behavioral outcomes.

Methods:
We analyzed data on 174 children from the Early Life Exposure in Mexico (ELEMENT) pregnancy and birth cohort in Mexico. Prenatal fluoride exposure was assessed as the average creatinine-adjusted maternal urinary fluoride concentration (MUFcr) across trimesters. Children's neurodevelopment was evaluated using 55 outcomes from infancy to early adolescence using standardized tests (Bayley, McCarthy, WASI, BASC-II, CPRS-R and CPT-II). Ninety-nine neurotransmission-related SNPs were genotyped in children. Longitudinal mixed-effects models evaluated main genetic effects and gene-fluoride interactions, adjusting for relevant covariates. False discovery rate (FDR) correction was applied using the Benjamini-Hochberg method.

Results:
Main-effect models identified 27 SNPs associated ($p < 0.1$) with ≥10 neurodevelopmental outcomes. Interaction models revealed three SNPs—rs1016732 (ATP1A2 gene), rs1943694 (DLG2 gene), and rs1799286 (GRIN2D gene)—that significantly modified fluoride-outcome associations. The rs1016732 AA genotype showed a protective effect, mitigating fluoride's impact, while rs1943694 TC and 1799286 CT genotypes were associated with greater risk. Significant interactions ($p <0.05$) involved behavioral domains—hyperactivity, emotional self-control, externalizing problems, ADHD index, and restless/impulsive (BASC-II and CPRS-R)—as well as cognitive outcomes like the General Cognitive Index (McCarty).

Conclusions:
The identified SNPs are located close to genes involved in ion homeostasis (ATP1A2), synaptic scaffolding (DLG2), and excitatory neurotransmission (GRIN2D), suggesting they may modulate susceptibility to prenatal fluoride's neurodevelopmental effects. Findings underscore the relevance of gene-environment interactions in shaping neurodevelopment and emphasize the need of evaluating genetic susceptibility in environmental health risk studies.

Funding:

Supported by the U.S. National Institutes of Health (NIH; grants R01ES021446 and R01ES007821), the National Institute of Environmental Health Sciences/U.S. Environmental Protection Agency (NIEHS/EPA; grant P01ES022844), and the NIEHS (grants P42ES05947 and P30ES017885, NIEHS Center Grant).

Key-words: (up to 5):

SNPs, Fluoride exposure, Neurodevelopment, ELEMENT cohort, Mixed-effects

Abstract #00006029 en

Multidimensional Socioeconomic Shifts and Childhood Obesity Risk in Chile (2009-2017): A DOHaD Perspective Using Bayesian Multiple Index Modeling

Impact of Early Life Exposures and Environmental Pollutants

Sepúlveda Peñaloza Alejandro (1), Urquidi Cinthya (1), Castro Rocio (1), Matus Patricia (1) (1) Universidad de los Andes

Background/aims:
Obesity disproportionately affects populations with low socioeconomic status (SES), with long-term implications for health outcomes. In Chile, rapid socioeconomic changes occurred between 2009 and 2017, potentially impacting early-life exposures and shaping obesity trajectories. This study analyzed the effect of the acceleration of change in multidimensional SES components, encompassing education, health, housing, residence, and employment, on obesity prevalence at sub-national levels during this eight-year period, considering the implications for developmental origins of health and disease (DOHaD).

Methods:
Multiple datasets from the National Health Surveys (NHS) and the Household Socioeconomic Surveys (CASEN) conducted in Chile between 2009 and 2017 were combined. We analyzed the change in various SES indicators within the education, health, housing, residence and employment modules across 29 health services (HS). The relationship between the acceleration of change in these SES indicators and obesity prevalence among adults and adolescents since the age of 15 was assessed using Quantile G-computation, Bayesian Multiple Index Models (BMIM), and Bayesian Kernel Machine Regression (BKMR). Variables included access to scholarships, nutrition status, subsidized housing, and income from other sources.

Results:
Quantile G-computation indicated that a greater increase in normal nutrition and access to scholarships was associated with lower obesity prevalence in health Services. A greater increase in household income from other jobs was associated with lower obesity prevalence. BMIM analysis identified the education and housing dimensions as the most important predictors of obesity prevalence patterns.

Conclusions:
This study reveals the complex relationship between the acceleration of change in socioeconomic factors and obesity prevalence in Chile between 2009 and 2017. These results highlight the importance of considering the dynamic nature of socioeconomic factors when designing interventions to prevent obesity and improve long-term health outcomes, in a DOHaD context.

Funding:
No funding

Key-words: (up to 5):
Bayesian mixture models, socioeconomic status, obesity, multiple exposures, social disparities

Abstract #00006044 en

Nutritional intervention during and after pregnancy reverses neuroendocrine disorders in adult offspring. What is the role of saturated fats?

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Barrera Cynthia (1), Valenzuela Carina (2), Llanos Miguel (3)
(1) University of Chile, (2) Universidad de Valparaiso, Chile, (3) Insituto de Nurición y Tecnología de los alimentos (INTA)

Background/aims:
Previous studies have linked maternal high-fat diet (HFD)-induced obesity with higher basal corticosterone levels in offspring, suggesting potential programming of the hypothalamic-pituitary-adrenal (HPA) axis. This study evaluated the impact of a reduced-fat nutritional intervention during pregnancy and lactation on adult offspring.

Methods:
The model considered three experimental groups, 45 days old female mice (C57/BL/6), separated according to diet: Group A: females with control diet before and during pregnancy and lactation; Group B: females with a HFD (fat: 60% Kcal) before and during pregnancy and lactation; Group C: females with a high-fat diet until mating and control diet (fat: 10% Kcal) in pregnancy and lactation. Males used for mating and respective offspring were fed a post-weaning control diet. Offspring (5 of each group) were sacrificed (120 days old), and blood samples were taken. Subsequently, basal corticosterone levels were determined using an ELISA kit. In addition, the fatty acid profile of the maternal diet was determined by gas chromatography. All treatment protocols for experimental animals were approved by the Bioethics Committee (No. PT2016-03-CB-ML).

Results:
Differences in basal corticosterone levels were observed, which were 40% higher in offspring of mothers on a high-fat diet compared with mothers on a control diet, and a 20% reversal in offspring of mothers on the intervention diet. Relating the grams of saturated fat in the maternal diet with corticosterone levels in the offspring showed a positive and moderate correlation (Spearman's Rho = 0.5341; p = 0.0492).

Conclusions:
A normalizing effect on basal corticosterone levels can be observed in children of mothers treated with a control diet, and this result is related to the saturated fat content of the maternal diet.

Funding:
Fondo Nacional de Desarrollo Científico y Tecnológico (FONDECYT) 1130106.

Key-words: (up to 5):
Nutritional intervention, pregnancy, corticosterone, saturated fat

Abstract #00006065 en

Maternal-fetal repercussions of pequi oil (Caryocar brasiliense Cambess) treatment during pregnancy in diabetic rats

Plant and Animal Health and Its Impact on Reproductive Age Individuals and Their Offspring

Campos Ribeiro Thais (1), Roberto da Silva Filho Paulo (1), Fernandes Camily (1), Vitor Alves Damacena João (1), Queiroz Moraes-Souza Rafaianne (1), Becker Pertuzatti Konda Paula (1), Cristina Damasceno Débora (2), Lopes da Cruz Larissa (1), Tadeu Volpato Gustavo (1)
(1) Universidade Federal de Mato Grosso, (2) Universidade Estadual de São Paulo

Background/aims:
The aim of this study was to evaluate the effects of Caryocar brasiliense oil administration during pregnancy in diabetic rats.

Methods:
(Ethics committee 23108.041305/2024-54). Diabetes was induced in Wistar rats by streptozotocin injection at 24 hours of life and confirmed at 110 days of age through the oral glucose tolerance test (OGTT). The rats were then mated and randomly divided into four experimental groups (n=13/group): non-diabetic (C e T) or diabetic (D) rats treated with water or C. brasiliense oil (D or DT). Pequi oil was administered orally (1000 mg/kg) from day 0 to 21 of pregnancy. Body weight, water and food intake were monitored weekly, and the OGTT was repeated on the 17th day of pregnancy. On the 21st day, the rats were anesthetized, and blood samples (for biochemical analysis) and uteri (for reproductive evaluation) were collected. Fetuses and placentas were weighed, and fetal anomalies were analyzed.

Results:
The Treated group showed a decrease in food intake (15.6±1,4) and increases in triglycerides (150.8±39.0), VLDL-c (30.1±7.8), HDL-c (35.7±1.5), and placental efficiency (12.1±1.8) compared to the Control group (17.6±1.7, 77.6±22.3, 15.5±4.5, 21.8±2.9, and 11.5±1.6, respectively). Fetuses from the diabetic group showed a higher incidence of visceral (26%) and skeletal (22%) anomalies compared to the non-diabetic animals (15 and 12%). Additionally, the area under the curve (AUC), and fetal weight were increased in both diabetic groups. However, pequi oil treatment reduced the AUC and placental weight (0,48±0,06), and increased placental efficiency (11,90±1,69) compared to the diabetic group (0,53±0,09, 10,81±1,87, respectively).

Conclusions:
Pequi oil treatment requires caution due to the presence of hyperlipidemia but appears to be a promising complement for therapeutic application.

Funding:
Coordination for the Improvement of Higher Education Personnel (CAPES - Finance Code 001) and the National Council for Scientific and Technological Development (CNPq).

Key-words: (up to 5):
Hyperglycemia. Hypertriglyceridemia. Pregnancy. Pequi. Rats.

Abstract #00006066 en

Breastfeeding status, birth weight, and maternal body mass index association with rapid weight gain: a prospective cohort study

Role of Infant and Young Child Feeding Practices on Long-Term Health

Campos Adriana Divina de Souza (1), Silva Gabriela Torres (1), Figueiredo Amanda Caroline Cunha (1), Polessa Paula Daniela (1), Schneider Bruna Celestino (1), Mucci Daniela de Barros (1), Islam M. Munirul (2), Moore Sophie E. (3), Mølgaard Christian (4), Michaelsen Kim F (4), Allen Lindsay H (5), Kac Gilberto (1)
(1) Nutritional Epidemiology Observatory, Rio de Janeiro Federal University, (2) International Centre for Diarrhoeal Disease Research, Bangladesh , (3) Department of Women and Children's Health, King's College London, (4) Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, (5) Department of Nutrition, University of California, Davis

Background/aims:
Breastfeeding status, birth weight (BW), and maternal body mass index (BMI) have been associated with rapid weight gain (RWG) in infancy, a key risk factor for later obesity. This study investigated the association between these factors and RWG.

Methods:
The Mother, Infant, and Quality (MILQ) study is a prospective multicenter cohort conducted in Bangladesh (n=233), The Gambia (n=62), Denmark (n=174), and Brazil (n=113), including 582 healthy mother-infant dyads followed at M1 (1.0–3.49 months), M2 (3.5-5.9 months), and M3 (6.0–8.5 months). Exclusive breastfeeding (EBF) status up to 6 months was classified according to WHO criteria (yes/no), based on maternal reports of when other foods were introduced. BW in grams was categorized into tertiles (1º: 2500–3000; 2º: 3003-3445, and 3º: 3448-4200), and maternal BMI was assessed at M1. RWG was defined as an increase in weight-for-age z-score ≥0.67 between M1 and M3. Multiple logistic regression models assessed the associations of EBF status, BW, and maternal BMI with RWG, adjusting for maternal age, infant sex, and parity. All sites received ethical approval, and informed consent was obtained (BG:
PR-17085; GB: 22768; DK: H-17015174; BR: 2.086.708).

Results:
RWG occurred in 18.9% (n=110) of infants, with higher prevalence in the lowest BW tertile (24.6%) versus the highest (11.0%). RWG was 16.4% in infants with EBF <6 months and 22.5% in those EBF for 6 months. EBF until 6 months increased RWG odds by 42% (OR=1.42; 95%CI: 1.09–1.84). Infants in the lowest BW tertile had 195% higher odds (OR=2.95; 95%CI: 2.10–4.18), and each 1 kg/m² increase in maternal BMI raised RWG odds by 5.6% (OR=1.05; 95%CI: 1.01–1.09).

Conclusions:
EBF until 6 months, lower BW, and higher maternal BMI are associated with increased odds of RWG, highlighting the complex interplay between maternal and infant factors in early growth.

Funding:
Bill & Melinda Gates Foundation (NCT03254329)

Key-words: (up to 5):
Nutritional status, infant growth, infant feeding practices.

Abstract #00006074 en

Prevalence of food allergy in Brazilian children under 5 years: Results from the Brazilian National Survey on Child Nutrition (ENANI-2019)

Public Health Policies Across the Life Cycle.

Freitas-Costa Nathalia (1), Souza Clara (1), Normando Paula (1), Damasceno Davi (1), Ferreira Yve (1), Golden Lucas (1), Rodrigues Driele (1), Rugani Inês (2), Kac Gilberto (1)

(1) Institute of Nutrition Josué de Castro, Federal University of Rio de Janeiro, (2) Institute of Nutrition, State University of Rio de Janeiro

Background/aims:

The global increase in food allergy (FA) prevalence has become a public health concern. This study estimated the prevalence of any FA, milk allergy (MA), and egg allergy (EA) according to sociodemographic characteristics and breastfeeding practices.

Methods:

We analyzed data from 14,558 children <5 years from the Brazilian National Survey on Child Nutrition (ENANI-2019). FA prevalence and 95% confidence intervals (CIs) were based on medical diagnoses (yes/no) and food type reported by the mothers/caregivers. Statistically differences in FA according to sociodemographic characteristics/breastfeeding practices were identified by non-overlapping 95%CIs. Associations between breastfeeding (yes/no) and FA were estimated through odds ratios (ORs) and 95%CIs using multiple Poisson regression. ENANI-2019 was approved by the ethics committee (CAAE:
89798718.7.0000.5257), with participation confirmed by guardian consent.

Results:

FA prevalence was 4.6% (95%CI: 4.0–5.3), higher among children aged 24–59 months [5.7 (4.8–6.5)] and those whose mothers/caregivers had ≥11 years of schooling [5.3% (4.6–6.1)], compared to 1–23 months [3.0% (2.1–3.8)] and 8–10 years of schooling [3.0% (2.0–4.0)]. MA prevalence was 2.1% (1.7–2.5), higher among children of mothers/caregivers with ≥11 years of schooling [2.5% (1.9–3.0)] vs. 8–10 years [1.1% (0.7–1.6)]. EA prevalence was 0.6% (0.4–0.9), also higher in ≥11 years of schooling [1.0% (0.6–1.3)], compared to those with 0–7 years [0.2% (0.0–0.4)]. No differences were observed by the child's race/skin color, sex, National Economic Indicator, daycare/school attendance, and cash transfer program participation. FA and MA were less prevalent among children breastfed the day before the interview [FA: 2.8% (1.9–3.8) vs. 5.4% (4.6–6.2); MA: 0.9% (0.6–1.3) vs. 2.6% (2.0–3.1)]. Breastfeeding was a protective factor for FA for children 0-23 months [OR: 0.40 (0.17–0.92)] but not for 24-59 months [OR: 1.17 (0.63–2.17)].

Conclusions:

FA prevalence was higher among older children and those with more educated mothers/caregivers, while breastfeeding is a protective factor.

Funding:

This work was supported by The Brazilian Ministry of Health [Grant/Award Number: Not Applicable] and the Brazilian National Research Council (CPNq) grant number 440890/2017-9.

Key-words: (up to 5):
food allergy; breastfeeding; national survey; sociodemographic factors

Abstract #00006077 en

Association between household food insecurity and early childhood development: Results from the Brazilian National Survey on Child Nutrition (ENANI-2019)

Public Health Policies Across the Life Cycle.

Freitas-Costa Nathalia (1), Melo Juliana (1), Schincaglia Raquel (2), Santos Isabel (1), Rugani Inês (3), Kac Gilberto (1)
(1) Institute of Nutrition Josué de Castro, Federal University of Rio de Janeiro, (2) Faculty of Nutrition, Federal University of Goiás, (3) Institute of Nutrition, State University of Rio de Janeiro

Background/aims:
Household food security (FI) is critical to meet children developmental needs in the first years of life. This study explored the association between household FI and early childhood development (ECD) in Brazilian children.

Methods:
Data from 12,568 children aged 1-59 months studied in the Brazilian National Survey on Child Nutrition (ENANI-2019) were analyzed. Household FI was assessed using the Brazilian Food Insecurity Scale (EBIA) and classified as food security ("no" to all answers), mild (1-5 'yes' answers), and moderate/severe FI (≥ 6 'yes' answers). ECD was evaluated using the Survey of Well-being of Young Children (SWYC). The graded response model was used to estimate the developmental age according to developmental milestones reached by each child. The developmental quotient (DQ) was calculated as the developmental age divided by chronological age (DQ=1: expected milestones; DQ <1 or >1: below or above age expectations). Prevalence, means, and 95% confidence intervals (CI) were used to describe the sample. Multiple linear regression models were estimated, with FI as the main exposure and DQ as the outcome. ENANI-2019 was approved by the ethics committee (CAAE: 89798718.7.0000.5257), with participation confirmed by guardian consent.

Results:
The prevalence (95%CI) of mild and moderate/severe FI was 38.2% (33.6-42.7) and 10.5% (8.9-12.0). The mean DQ was 1.01 (0.99-1.03) and was higher among children living in food security households [1.04 (1.01-1.07)] compared to those with any level of FI [0.97 (0.95-0.99)]. The majority of children living in FI households had DQ below expectations for age [mild FI: 59.6% (56.2-63.0) and moderate/severe FI 62.7% (56.2-69.2)]. Mild and moderate/severe FI were inversely associated with DQ [mild: β=-0.05; 95%CI: -0.08;-0.01; p=0.006; moderate/severe: β=-0.06 95%CI: -0.11;-0.01; p=0.017), even after adjusting for confounders.

Conclusions:
Household FI was associated with lower DQ among Brazilian children. These findings highlight the importance of public policies ensuring food security to support optimal ECD outcomes.

Funding:
This work was supported by The Brazilian Ministry of Health [Grant/Award Number: Not Applicable] and the Brazilian National Research Council (CPNq) grant number 440890/2017-9.

Key-words: (up to 5):
Food Insecurity; Early childhood development; National Survey; Child Development.

Abstract #00006092 en

Effect of a nutritional counselling on biochemical profile during pregnancy, and its relation with ultra-processed food consumption

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

de Lima Maria Carolina (1), Carreira Natalia Posses (1), Sartorelli Daniela Saes (1) (1) Faculty of Medicine of Ribeirão Preto, University of São Paulo

Background/aims:
Metabolic changes are physiologically verified during pregnancy. However, when exacerbated, it might affect infant health. This study evaluated the effect of nutritional counselling during pregnancy on the biochemical profile of pregnant women and whether these changes were related to food consumption according to the Nova food classification.

Methods:
Randomized controlled trial conducted in Primary Care in a Brazilian municipality between 2018 and 2021. Adult pregnant women with pre-gestational overweight (n=350) were randomized to the control (CG) and intervention (IG) groups. The intervention consisted of three individualized nutritional counselling sessions based on the Nova food classification system and encouraging physical activity. Fasting blood samples were taken up to the 15th gestational week (GA) and between the 34th and 36th GA. Food consumption was assessed using 24-hour dietary recalls. The Wilcoxon and Mann-Whitney tests were used for intra-group and inter-group analyses, respectively, and Quantile Regression was applied to investigate the relation with food consumption.

Results:
In the second assessment, GI had higher median total cholesterol (TC) and LDL-c compared to CG [245.00 (209.50; 270.00) vs. 224.00 (195.00; 255.00) p=0.03 and 143.00 (112.50; 169.50) vs. 115.00 (95.00; 153.50) p=0.004, respectively]. In the CG, consumption of unprocessed and minimally processed foods was associated with lower TC (-1.55 mg/dL at P25) and LDL-c (-1.45 mg/dL at P50 and -1.78 mg/dL at P75). In contrast, consumption of ultra-processed foods was associated with higher TC (2.64 mg/dL at P25; 1.97 mg/dL at P50 and 1.27 mg/dL at P75) and LDL-c (1.36 mg/dL at P25; 2.25 mg/dL at P50 and 2.10 mg/dL at P75).

Conclusions:
The intervention's effect on the lipid profile was unexpected. However, a higher ultra-processed food intake was directly related to the TC and LDL in CG, showing that the biochemical changes observed were inherent to the pregnancy and not due to the counselling.

Funding:
Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) 2017/15386–2, 2017/18980–2 e 2021/06468-0; Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) 406000/2018–2, 302487/2018–2; Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) e Fundação de Apoio ao Ensino, Pesquisa e Assistência do Hospital das Clínicas da Faculdade de Medicina de
Ribeirão Preto da Universidade de São Paulo (FAEPA) 1039/2018, 1114/2018, 61/2019, 62/2019 e 754/2021.

Key-words: (up to 5):

Pregnancy, Overweight, Biomarkers, Nova classification, Randomized Controlled Trial

Abstract #00006098 en

Molar-Incisor Hypomineralization, a Perinatal Enamel Condition that Increases Caries Severity in Adolescents: Population-Based Study

Big Data and Cohorts in DOHaD Research.

ALVES CLAUDIA MARIA COELHO (1), Franco Marcela Mayana Pereira (2), Costa Elisa Miranda (3), Thomas Erika Bárbara Abreu Fonseca (3), Ribeiro Cecilia Claudia Costa (2)

(1) Postgraduate Program in Dentistry, Federal University of Maranhao, São Luís, Maranhão, Brazil, , (2) Postgraduate Program in Dentistry - Federal University of Maranhao, São Luís, Maranhão, Brazil, , (3) Postgraduate Program in Public Health - Federal University of Maranhao, São Luís, Maranhão, Brazil

Background/aims:

Molar-incisor hypomineralization (MIH) is a developmental enamel defect linked to stressors during the pre- and perinatal periods. This study investigated MIH as an exposure associated with increased caries severity indicators, such as the DMFT index and pulpal involvement of carious lesions (PUFA) in adolescents.

Methods:

The study used data from a birth cohort, examining 2,515 adolescents aged 18–19. Sociodemographic and behavioral data were collected through a standardized questionnaire. Clinical examination assessed the main exposure (MIH) and outcomes: untreated dental caries, DMFT index, and PUFA index. Descriptive analysis and Chi-square tests were used to compare exposed and unexposed groups. Associations were estimated using Poisson regression, with adjusted and unadjusted models ($\alpha \leq 0.05$). Socioeconomic confounders were selected using a directed acyclic graph (DAG). All participants gave written consent (Ethics Commitee # CAAE 49096315.2.0000.5086, process number 1.302.489)

Results:

The prevalence of MIH was 15.43% (n=453). Untreated dental caries was found in 63.35% of the sample, the mean DMFT was 3.70, and PUFA prevalence was 18.28%. Poisson regression showed that MIH was associated with untreated caries in both unadjusted (PR=1.25, p≤0.001) and adjusted analyses (PR=1.28, p≤0.001). A significant association was also found between MIH and DMFT in both unadjusted (PR=1.01, p≤0.001) and adjusted models (PR=1.01, p≤0.001). No significant association was observed between MIH and PUFA, either in unadjusted (PR=0.95, p=0.282) or adjusted analyses (PR=0.94, p=0.272).

Conclusions:

MIH, a developmental enamel defect originating in the pre-and perinatal periods, can have repercussions on oral health in the future, increasing the caries burden during adolescence.

Funding:

This work was supported by Brazilian Ministry of Health/Department of Science and Technology (DECIT), the Foundation for the Support of Research and Scientific and Technological Development of Maranhão (FAPEMA; the Coordination for the Improvement of Higher Education Personnel (CAPES; Finance Code 001) and National Council for Scientific and Technological Development (CNPq).

Key-words: (up to 5)

Epidemiology; Adolescence; Dental Caries. Molar-incisor hypomineralization

Abstract #00006138 en

Risk Factors for Gestational Diabetes Using Explainable Machine Learning in a Chilean Population

Big Data and Cohorts in DOHaD Research.

Lazo Sofía (1), Fossa Matías (1), Pardo Fabián (1), Salas Rodrigo (1), Bertini Ayleen (1) (1) Universidad Valparaíso

Background/aims:
Gestational diabetes mellitus (GDM) affects 10% of pregnancies in Chile, with significant maternal-fetal complications. This study developed an explainable machine learning (ML) model using pregestational and gestational data from women delivering at Hospital San Camilo (2015-2021) to predict GDM risk and identify key modifiable factors in Chile's Valparaíso region.

Methods:
We analyzed 11197 clinical records using XGBoost with SHAP (SHapley Additive exPlanations) for interpretability. Key variables included age, parity, pre-existing diabetes, education level, and healthcare access category. Data preprocessing involved:
-Standardization of categorical variables (marital status, education)
-Handling missing values
-Creation of dummy variables
-80/20 train-test split with stratified 10-fold cross-validation

Results:
The model achieved strong performance (AUC: 0.83; sensitivity: 0.80; F1-score: 0.81).
SHAP analysis revealed:
-Pre-existing diabetes as the strongest predictor (highest positive SHAP values)
-Age and higher education as secondary significant factors
-Complex interactions between socioeconomic variables (healthcare access) and biological factors
The model showed excellent specificity (99%) but slightly lower sensitivity (79%) for GDM cases, with robust cross-validation results (mean precision: 0.97).

Conclusions:
This explainable ML approach successfully identified both clinical (pre-existing diabetes) and socioeconomic (education, healthcare access) risk factors for GDM in Chilean women. The model's interpretability enables:
-Personalized risk assessment for clinical practice
-Targeted public health interventions -Future integration of psychosocial variables

Funding:
No fundings

Key-words: (up to 5):

gestational diabetes, explainable AI, predictive modeling, pregnancy, Latin America

Abstract #00006150 en

The founder generation of a mouse model of multigenerational paternal exposure to arachidonic acid displays alterations of the testis DNA methylome and transcriptome.

Mechanisms Determining Transgenerational Effects of Health and Disease

Marquez Nuria Areli (1), Sánchez Palafox Jaime Eduardo (1), Correa Navarro Viridiana Abigail (1), Romo Morales Gloria del Carmen (1), Andrade Pacheco Isaí Andrés (1), Sánchez García Leslie Yadira (2), Rodríguez Ríos Dalia (3),
Fierro Pastrana Reyna Carmen (4), Zaina Silvio (1), Lund Gertrud (3)
(1) University of Guanajuato, (2) Humani Mundial University, (3) CINVESTAV, (4) Metropolitan Autonomous University

Background/aims:
Arachidonic acid (AA) is a bioactive polyunsaturated fatty acid. In addition to its crucial role in fetal brain development, AA is the precursor of inflammatory response modulators. Paternal AA supplementation across three consecutive generations triggers physiological changes that are detectable in a fourth unexposed generation in mice. The data suggest an intergenerational molecular memory of paternal AA exposure, resulting in cumulative effects. To elucidate the underlying molecular events, we are surveying the DNA methylome and transcriptome of the AA-exposed reproductive system and selected non-reproductive organs in the aforementioned mouse model of multigenerational paternal AA exposure. Here, we present a description of our initial findings in the testis of the founder generation - i.e. descendant of unexposed mice.

Methods:
Founder generation twelve-week old male C57BL/6 mice were orally supplemented with 1.35 mg AA (Sigma) or vector (soybean oil; n=12/group) daily for 10 days. The testis was dissected two days post coitum. DNA and RNA were extracted for DNA methylation (Infinium Mouse Methylation BeadChip, Illumina) and transcriptome (M22K Chip, UNAM, Mexico) analysis, respectively. The relevant institutional ethical committee has approved the study (approval ID: CEPIUG-P45-2023).

Results:
AA-induced differential DNA methylation (threshold: >20% methylation difference; t-test $p<0.001$) was limited to four loci implicated in lipid metabolism, all tightly clustered in chromosome 18. AA induced a transcriptional signature characterized by overexpression (>3-fold) of genes that promote the immune response including Tnf, Cxcl16, C1ra, Trav3-3 and Unc93b1.

Conclusions:
AA supplementation in founder males may impact the molecular information carried by the sperm and induce the observed intergenerational effects, through the activation of immune response-promoting genes in the testis. Further studies will assess whether those responses to paternal AA are amplified in subsequent generations, and their functional impact.

Funding:
SECIHTI (Mexico) "Ciencia de Frontera" Programme, grant no. CF-2023-G-252.

Key-words: (up to 5):

Arachidonic acid, DNA methylation, paternal inheritance, sperm, trascriptome

Abstract #00006155 en

Extracellular Vesicles in the Breastmilk from Women with Polycystic Ovary Syndrome: Preliminary Associations with Infant Body Composition

Role of Infant and Young Child Feeding Practices on Long-Term Health

Leiva Carla (1), Sánchez Francisca (2), Aguilera Gonzalo (3), Atencio Camila (4), Valenzuela Rodrigo (2), Jorquera Pia (5), Maliqueo Manuel (2)

(1) Universidad de Chile/ Pontificia Universidad Católica, (2) Universidad de Chile, (3) Univesidad de Chile, (4) Universidad de Chile/INTA, (5) HCSBA

Background/aims:

Extracellular vesicles (EVs) contained in human breastmilk are key mediators of maternal-infant communication, influencing infant body composition. Moreover, they are modified in maternal conditions such as obesity and gestational diabetes. However, EVs from the breastmilk of women with polycystic ovary syndrome (PCOS), a common endocrine-metabolic disorder at reproductive age, have not been studied. Therefore, we analyzed EVs contained in the breastmilk of women with PCOS.

Methods:

Breastmilk samples were collected from 24 lactating women (6 with PCOS and 18 controls).

EVs were isolated using low-speed centrifugation, followed by filtration and size-exclusion chromatography (SEC). Particle size and concentration were analyzed via Nanoparticle Tracking Analysis (NTA). Infant nutritional status was assessed through weight, length, mid-upper arm circumference, and 4–5 skinfolds, allowing estimation of body fat percentage using modified Slaughter and Goran equations, and z-scores for weight/length and BMI-for-age. Maternal variables (BMI, fasting insulin, HOMA-IR) and infant feeding type were also recorded. Pearson correlations were computed by group. All participants gave written consent (Ethics Committee #084-2024).

Results:

Most infants were exclusively or predominantly breastfed. Breastmilk from women with PCOS showed higher EV concentration than control ($4.68 \times 10^{10} \pm 3.84 \times 10^{10}$ vs. $8.74 \times 10^{10} \pm 4.39 \times 10^{10}$ particles/mL; $p = 0.039$). No differences in mean or modal EV size were observed. Infant anthropometric parameters and body fat percentage were similar between groups. In the PCOS group, a negative association was found between EV size and infant fat percentage ($r = -0.709$). A negative correlation between EV size and maternal insulin was also noted ($r = -0.609$). However, none of these correlations reached statistical significance.

Conclusions:

These findings support the hypothesis that the physical characteristics of milk-derived EVs may reflect maternal metabolic status and relate to early markers of infant body composition. Further analysis, such as miRNA transcriptome profiling, could provide insights into their role in postnatal growth.

Funding:

Proyecto SOCHINUT - Henry Nestlé 2023, Proyecto Sociedad Chilena de Endocrinología y Metabolismo (SOCHED) 2023, ANID Becas/Doctorado Nacional 21220507, Fondecyt regular 1241725.

Key-words: (up to 5):
Breastmilk, extracellular vesicles, polycystic ovary syndrome (PCOS), and infant body composition.

Abstract #00006193 en

Establishment of the gut microbiome in infants born prematurely is associated with exposure to stress-inducing medical procedures

Impact of Early Life Exposures and Environmental Pollutants

Mercer Emily (1), Piché-Choquette Sarah (2), Gorospe Julia (1), Rangipour Zahra (1), Asbury Michelle (1), Alshaikh Belal (1), Lacaze-Masmonteil Thierry (1), Sycuro Laura (1), Kembel Steven (2), Giesbrecht Gerald (1), Arrieta
Marie-Claire (1)
(1) University of Calgary, (2) University of Québec

Background/aims:
The gut microbiome is a diverse microbial community capable of influencing early human development via gut-brain communication networks. Animal models have demonstrated a causal relationship between early-life stress and microbiome disruptions in early life; however, clinical evidence remains limited. Preterm infants provide a unique opportunity to explore these interactions given their distinct microbiome profiles and frequent exposure to stress-inducing medical interventions in the neonatal intensive care unit (NICU), suggesting altered gut-brain communication may contribute to the developmental outcomes observed in this population. In this work, we evaluated the relationship between the maturation of the gut microbiome, cortisol levels, and clinical exposures (e.g., stress-inducing interventions) over the first 60 days of life in 105 preterm infants from the Alberta BLOOM Study.

Methods:
Weekly stool and urine samples were collected from infants over the first 60 days of life. Bacterial microbiome composition was determined by shallow shotgun sequencing. Urine cortisol levels were measured by ELISA. Clinical data (e.g., nutrition, medications, stress-inducing interventions) was obtained from hospital charts. Ecological and multivariate analyses were conducted in R. Written consent was obtained from participants' caregivers (REB17-1877 & REB20-1442).

Results:
Gut microbiome maturation varied by gestational age, with extremely preterm infants exhibiting lower alpha diversity and enrichment of opportunistic microbes (e.g., Klebsiella, Staphylococcus). Alpha and beta diversity were positively associated with probiotic supplementation and negatively associated with antibiotics and cumulative stress exposure (i.e., stress-inducing procedures, invasive ventilation). Cumulative stress exposure was linked to increased abundances of opportunistic genera and a reduction in beneficial commensals (e.g., Bifidobacterium). Associations between the microbiome and urine cortisol were limited.

Conclusions:
Our findings suggest a dynamic relationship exists between gut microbiome maturation and early-life stress in preterm infants, highlighting the potential developmental impacts of stress-inducing interventions endured in the NICU via the gut-brain axis.

Funding:
CIHR #429655

Key-words: (up to 5):

Gut microbiome, gut-brain axis, preterm infants, early-life stress, cortisol

Abstract #00006194 en

Kefir Prevents Colorectal Cancer via Butyrate-Independent Mechanism in Neonatal Overfeeding Model

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Ávila Alpino (1) Gabriela de Cássia (1), Guiomar de Almeida Brasiel (1) Poliana (1), Macedo de Almeida (2) Mariana (2), Nascimento Barreto (1) Eduardo (1), Alves da Silva (1) Thiago (1), Vianelo Netto Rezende (1) Luan (1), Cristina Potente Dutra Luquetti (1) Sheila (1)
(1) (1) Departamento de Nutrição, Universidade Federal de Juiz de Fora (UFJF), (2) (2) Departamento de Farmacologia, Universidade Federal de Juiz de Fora

Background/aims:
Colorectal cancer (CRC) is a prevalent cancer worldwide, with obesity being a key risk factor. Neonatal overfeeding induces obesity in adulthood, characterized by increased adiposity, chronic inflammation, and gut dysbiosis, all of which may contribute to CRC development. Short-chain fatty acids (SCFAs), especially butyrate, exert anti-inflammatory and anticancer effects by enhancing the intestinal barrier and promoting cancer cell apoptosis. We aimed to investigate the impact of kefir, a probiotic source, on adiposity, tumorigenesis, and SCFA levels in a neonatal overfeeding-induced model of CRC.

Methods:
All animal procedures were approved by the UFJF ethics committee (no. 21/2016). Rats were divided into four groups: Normal Litter (NL), Kefir Normal Litter (KNL), Small Litter (SL), and Kefir Small Litter (KSL), with neonatal overfeeding induced by reducing litter size (3 pups for SL, 10 for NL). During lactation, dams were gavaged with 1 mL of kefir or water daily. After weaning, pups continued their respective treatments until 60 days old. CRC was induced at 67 days using 1,2-dimethylhydrazine. At 240 days, animals were euthanized, visceral adiposity was measured, SCFAs analyzed from cecum feces by high performance liquid chromatography, and tumor numbers in the colon were investigated through aberrant crypt foci count.

Results:
The SL groups exhibited increased visceral adiposity ($p=0.0102$), tumor numbers ($p = 0.0102$), and surprisingly higher levels of SCFAs, with a significant rise in butyrate ($p = 0.0091$). Kefir intervention resulted in a reduction of adiposity (-20.04%; $p < 0.01$) and tumor incidence (-71.43%; $p < 0.01$) in the SL groups, but did not affect SCFA concentrations in these animals.

Conclusions:
Kefir showed a butyrate-independent protective effect in the neonatal overfeeding-induced CRC model. Neonatal overfeeding increased cecum levels of butyrate without protection against tumorigenesis, suggesting the butyrate use as a tumor energy source and/or reduced local responsiveness.

Funding:
FAPEMIG

Key-words: (up to 5):
Kefir, Butyrate, Colorectal Cancer (CRC), Adiposity, Neonatal Overfeeding

Abstract #00006234 en

Predicting early consumption of ultra-processed foods by children in the first 1000 days using machine learning

Big Data and Cohorts in DOHaD Research.

Viola Poliana Cristina de Almeida Fonseca (1), Sá Rafaela Vitória Pereira (1), Carvalho Carolina Abreu de (1), Costa Silas Alves (1), da Silva Millyam Karem Mariano (1), Thomaz Erika Barbara Abreu Fonseca (1), Feres Bruno (1), de Almeida Cecilia Claudia Costa Ribeiro (1) (1)
Universidade Federal do Maranhão (UFMA)

Background/aims:
Early exposure to ultra-processed foods (UPFs) has been associated a adverse health outcomes later in life. Identifying predictors of early UPF consumption during the first two years—a critical period—may support preventive strategies. The aim of this study is to predict the risk of early consumption of ultra-processed foods (UPF) among children under two years of age based on prenatal and postnatal factors, using a machine learning technique.

Methods:
Using data from BRISA prenatal cohort, São Luís, Brazil comprising 740 participants with complete data regarding UPF consumption. The outcome is defined as the consumption of foods with UPF greater than 20% of the diet of children aged 13 to 35 months. The prenatal and postnatal factors were chosen based on existing literature. Machine learning techniques were applied, the Support Vector Machine algorithm was used to build the model and SHapley Additive exPlanations (SHAP) to estimate the contribution of each predictor to the outcome. All participants gave written consent (Ethics Committee #4771/2008-30).

Results:
Children consuming more than 20% of UPF in their diet was 62.3%. Accuracy was 55.5% (CI95%: 51.8; 59.1); Sensitivity of 55.5%, specificity of 55.5%, F1 score of 0.60. Breastfeeding duration of less than 12 months was the main factor that contributed to the prediction of UPF consumption, followed by pre-gestational obesity, vaginal discharge, higher maternal education, maternal UPF consumption and maternal marital status (no partner). Unexpectedly, maternal smoking showed an inverse behavior in the model, but with a low contribution according to SHAP value.

Conclusions:
Machine learning proved useful in identifying predictors of early UPF consumption. Breastfeeding duration and maternal behaviors emerged as important predictors, highlighting opportunities for interventions in the first 1000 days to prevent future disease.

Funding:
This work was supported by the Brazilian Ministry of Health/DECIT/CNPq [no. 400759/2024-1] in partnership with the Gates Foundation.

Key-words: (up to 5):
Machine Learning; Ultraprocessed foods; Breastfeeding; Prenatal Care

Abstract #00006235 en

Tissue-Specific Expression-Based Polygenic Risk Scores and Methylation Score in Interaction with Birth Weight Associate to Childhood BMI: A Multi-Cohort Study

Mechanisms Determining Transgenerational Effects of Health and Disease

Lima-Soares Fernanda (1), Moscoso dos Santos Eduardo (2), Elgbelli Guillaume (3), Pokhvisneva Irina (3), Hian Tan Kok (4), Kok Yen Jerry (5), Pelufo Silveira Patrícia (3), de Andrade Paes Antonio Marcus (1)
(1) Health Sciences Graduate Program, Federal University of Maranhão , (2) Federal University of Maranhao, (3) Douglas Mental Health University Institute, McGill University, (4) SingHealth Duke-NUS Medical School, NIHR Southampton Biomedical Research Centre, (5) Department of Reproductive Medicine, KKWomen`s and Children`s Hospital, Singapure

Background/aims:
Poor fetal growth, measured primarily through birth weight, is a common prenatal adversity that triggers neurometabolic alterations, including altered eating behavior and increased obesity risk later in life.
However, individual differences exist; not all children exposed to this adversity will develop obesity.

Methods:
We used data from a discovery epigenetic wide association study (EWAS) of adult body mass index (BMI) (Do et al., 2023) to calculate a methylation score in three child cohorts with methylation data: MAVAN (Canada), n = 87, age 6; GUSTO (Singapore), n = 289, ages 6 and 12 months; and BIBO (Netherlands), n = 124, age 6. Using genotype data from these children, we also calculated expression-based polygenic risk scores (ePRS) based on gene expression informed by GTEx data in the nucleus accumbens (NAcc) and white adipose tissue (WAT). We tested whether these ePRSs moderated the association between birth weight and BMI, and whether adding the methylation score improved the models.

Results:
In MAVAN, there was a significant interaction between NAcc ePRS and birth weight on BMI at 6 years, detected with (β = -0.0008, $p < 0.05$) and without the methylation score. In GUSTO, WAT ePRS interacted with birth weight on BMI at 6 (β = -0.0004, $p < 0.05$) and 12 months (β = -0.0002, $p < 0.05$), regardless of methylation score inclusion. No interactions were observed in BIBO.

Conclusions:
Birth weight interacted with distinct tissue-specific ePRSs across populations. Although the ePRSs were derived from the same gene set, their predictive value for BMI in childhood was influenced by the tissue gene expression weight and population-specific factors such as ethnic background. These findings underscore the need to consider population diversity when evaluating susceptibility to prenatal adversity.
Such insights are critical for advancing precision prevention strategies in early metabolic health.

Funding:
CAPES and CNPQ

Key-words: (up to 5):
functional genomics; ePRS; birth weight; BMI; DOHaD

Abstract #00006251 en

Predicting childhood overweight from prenatal factors using machine learning

Big Data and Cohorts in DOHaD Research.

ABREU FONSECA THOMAZ ERIKA BARBARA (1), SÁ RAFAELA VITORIA PEREIRA (1), Viola Poliana Cristina de Almeida Fonseca (1), JARDIM ANA TAMIRES (1), RIBEIRO CECILIA CLAUDIA COSTA (1)
(1) FEDERAL UNIVERSITY OF MARANHAO

Background/aims:
Childhood weight excess is a significant public health problem associated with metabolic dysfunctions later in life. Using a machine learning technique, this study aims to predict the risk of developing overweight at two years of age based on maternal variables during pregnancy.

Methods:
Data were drawn from the BRISA prenatal cohort, including complete overweight information for 1128 mother-child pairs. Overweight was defined as a BMI-for-age z-score ≥2.00 at two years of age. A set of maternal variables was subjected to univariate selection using the chi-square test, resulting in three variables reaching statistical significance ($p < 0.05$). These selected variables were subsequently employed to build a predictive model using the Random Forest algorithm. For model interpretability, SHapley Additive exPlanations (SHAP) was applied. All participants gave written consent (Ethics Committee #4771/2008-30).

Results:
Overweight prevalence at two years of age was 11.97%. The selected variables included maternal age, pregestational obesity, periodontitis, head of the family occupation, number of people in the household, and early introduction of formula feeding. Model accuracy was 60.6% (CI95% 53.3; 61.6), with 53.3% sensitivity and 61.3% specificity. According to SHAP analysis, early formula introduction, pregestational obesity, periodontitis, and a high-skilled head of household emerged as main predictors for the outcome.
Intermediate maternal age (between 18 and 35) was also associated with increased risk.

Conclusions:
Early formula introduction, along with conditions such as obesity and periodontitis during pregnancy, were predictive of overweight development at the second year of life. These findings underscore the need for focused attention on the nutritional and metabolic conditions during pregnancy and on infants who require formula feeding to avoid the onset of overweight in early life.

Funding:
This work was supported by: 1) the Brazilian Ministry of Health/DECIT/CNPq in partnership with the Gates Foundation [no. 400759/2024-1]; 2) CNPq [Nº 441882/2023-4 and 308917/2021-9]; and CAPES [finance code 001].

Key-words: (up to 5):
Artificial intelligence; Machine Learning; Overweight; Prenatal Care

Abstract #00006265 en

Increased NPC1 and StARD3 expression in placentas from women with MSPH promotes lysosomal and mitochondrial dysfunction

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Campos Fabian (1), Zanlungo Silvana (2), Illanes Sebastián (3), Leiva Andrea (1), Yañez Maria Jose (4)
(1) Facultad de Ciencias, Universidad San Sebastián, (2) Facultad de Medicina, Pontificia Universidad Católica de Chile, (3) Facultad de Medicina, Universidad de los Andes, (4) Universidad San Sebastián

Background/aims:
During the progress of human pregnancy, the concentrations of total cholesterol (TC) rise to maternal physiological hypercholesterolemia (MPH). However, in some cases, mainly for unknown reasons, the TC levels are increased far beyond the physiological range, which is referred to as maternal supraphysiological hypercholesterolemia (MSPH). Maternal-to-fetal cholesterol trafficking is poorly understood. The prevalence of MSPH is ~ 30% in a group of Chilean pregnant women and increased TC levels promote endothelial dysfunction and is associated with the development of cardiovascular disease in the offspring later in life, although the precise involved mechanisms are unknown. Classically, after receptor-mediated uptake of LDL, the particle is transported to the endosome/lysosome pathway via NPC1 and STARD3, which transfers cholesterol from the lumen of the lysosome to the mitochondria. Considering that TC levels are increased in maternal MSPH, we evaluated possible structural and functional alterations in the lysosome and mitochondria in syncytiotrophoblast cells exposed to increased TC levels or MSPH placentas.

Methods:
We used BeWo cells treated with ox-LDL (50-100 mg/mL, 24 h), and placentas from women with MPH or MSPH pregnancies. We evaluated intracellular cholesterol accumulation, and the structure and function of lysosomes and mitochondria in cells exposed to increased TC levels by RT-qPCR, Western Blot, Immunofluorescence, PFO-GST staining, and Lyso tracker Red, Mito tracker Green and Magic Red fluorescent probes

Results:
We found: i) an increase in intracellular levels of free cholesterol; ii) an increase in proteins involved in cholesterol transport and mitochondrial dynamics, iii) lysosomal dysfunction, and iv) a decreased ROS and ATP content in BeWo cells treated with ox-LDL and in the placentas from women with MSPH.

Conclusions:
MSPH is associated with changes in the expression of the proteins involved in cholesterol transport, which could have an impact on lysosomal and mitochondrial function in the syncytiotrophoblast cells.

Funding:
FONDECYT N°11200592 and N°1251012 (MJY), and N°1230527 (AL).

Key-words: (up to 5):
Pregnancy, cholesterol, lysosomal, mitochondrial dysfunction.

Abstract #00006305 en

Optimizing Human Milk Analysis: Microscale Methods vs. Automated Mid-Infrared Spectroscopy for Macronutrient Determination

Role of Infant and Young Child Feeding Practices on Long-Term Health

Hernandez-Guerrero Paula Axicalli (1), Díaz-Fernández Karla Denisse (1), Lomas-Soria Consuelo (1), Zambrano-González Elena (2), Ibáñez-Chávez Carlos Alberto (2)
(1) Departamento de Biología de la Reproducción, Instituto Nacional de Ciencias Médicas y Nutrición SZ, (2) Biol Reproducción, Instituto Nacional de Ciencias Médicas y Nutrición SZ/Facultad de Química, UNAM

Background/aims:
While standardized protocols exist for food macronutrient analysis, methods for breast milk remain variable and lack clear guidelines. Mid-infrared (MIR) spectroscopy, as used in human milk analyzers is widely applied for rapid, non-destructive macronutrient assessment. However, the limited volume and unique properties of early lactation milk can challenge MIR-based accuracy. In such cases, validated microscale methods offer a reliable alternative for quantifying protein, fat, and total solids. We aimed to assess the agreement between microscale methods and mid-infrared spectroscopy for breast milk macronutrient analysis, and their suitability in low-volume or challenging samples.

Methods:
Fifteen breast milk samples were collected from individual donors at different lactation stages (7 days to 12 months postpartum). Microscale methods (Bradford for protein, Folch for fat, and gravimetry for total solids—were compared with crude protein, fat, and total solids determined by Miris Human Milk Analyzer (Miris HMA). Agreement was assessed between microscale/gravimetric methods vs Miris HMA determinations using Deming regression (linearity and proportional differences), correlation coefficients (association strength), and Bland-Altman analysis (mean difference and limits of agreement) to evaluate systematic differences and consistency. Institutional ethical standards for human research were met.

Results:
For protein, agreement with Bradford was good ($r=0.78$; $y=1.18x–0.12$; $p=0.43$), with a mean difference of 0.04 g/dL (limits: –0.4 to 0.5). For fat, agreement with Folch was excellent ($r=0.96$; $y=0.98x+0.77$; $p=0.77$), with a mean difference of 0.69 g/dL (limits: –0.2 to 1.6). For total solids, correlation with gravimetry was strong ($r=0.94$; $y=0.92x+1.01$; $p=0.42$), with a negligible mean difference of 0.003 g/dL (limits: –1.2 to 1.2). No significant proportional or systematic differences were observed.

Conclusions:
Microscale methods showed strong agreement with MIR-based analysis and may serve as valid alternatives, especially for precious samples with limited volume or when milk consistency challenges the effectiveness of infrared techniques.

Funding:
FPIS2023-INCMN-5130/ FUNSALUD México

Key-words: (up to 5):
Breastfeeding, Breastmilk composition, Early nutrition, Infrared spectroscopy

Abstract #00006310 en

Resveratrol ameliorates ethanol-induced paternal germline toxicity and offspring developmental deficits

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Gotfryd Lucila (1), Cambiasso Maite Yael (1), Calvo Juan Carlos (1), Fontana Vanina Andrea (1) (1) IBYME

Background/aims:
Ethanol consumption impairs male fertility and offspring health. Resveratrol's potential to counteract these effects remains unclear. This study investigated whether resveratrol reverses ethanol-induced sperm/testicular damage and paternal transmission of developmental deficits.

Methods:
Adult male mice (Mus musculus, CrlFcen:CF1) were divided into: Control (water + vehicle), Et (15% ethanol + vehicle), Res (water + resveratrol 20 mg/kg), and EtRes (15% ethanol + resveratrol). Ethanol was administered ad libitum and resveratrol/vehicle was given via esophageal gavage for 12 days, followed by two days of water ad libitum. Sperm morphology, testicular histopathology, and DNA fragmentation (TUNEL assay) were assessed (n=5 males per group). Males were mated with naïve females; offspring weight and motor development were evaluated.

Results:
Ethanol impaired sperm head/tail morphology ($p < 0.05$), which resveratrol prevented. Testes exhibited elevated DNA fragmentation in seminiferous tubules ($p<0.05$) and Leydig cells ($p<0.01$), along with ethanol-induced seminiferous tubule damage ($p<0.01$); all of these effects were mitigated by resveratrol. In offspring, ethanol-exposed sires produced female pups with lower body weight ($p<0.05$), an effect reversed by paternal resveratrol supplementation. Male offspring from ethanol-exposed fathers showed delayed motor development, with impaired geotaxis ($p<0.05$) and air righting reflexes ($p<0.01$), and vertical screen test ($p<0.05$). Resveratrol treatment effectively normalized these motor deficits, though it did not improve performance in the vertical screen test.

Conclusions:
Ethanol compromises sperm morphology, testicular structure, and germ cell DNA, while also impairing offspring motor development and growth. Resveratrol partially protects against these effects, restoring sperm/testicular health and offspring phenotypes. These findings highlight the potential of resveratrol as a therapeutic agent against ethanol-induced developmental impairments in offspring.

Funding:
Fundación Honorio Bigand, Fundación Williams, Fundación Barón, and PICT 2021-GRF-TI00735.

Key-words: (up to 5):
Paternal ethanol exposure; Paternal inheritance; Resveratrol; Offspring neurodevelopment.

Abstract #00006348 en

Modifiable obstacles to healthy eating during pregnancy and their relation to gestational weight gain in Chilean primary care.

Mechanisms Determining Transgenerational Effects of Health and Disease

Pardo Fabian (1), Rodríguez Andrea (2), Gutiérrez Jaime (3), Moya Jessica (4), Pino Maricela (5), Palma Virla (6), Bertini Ayleen (7), Chiarello Delia I (7)

(1) Escuela de Medicina, Campus San Felipe, Universidad de Valparaíso, (2) Instituto de Salud Pública de la Universidad San Sebastián, (3) Escuela de Tecnología Médica, Facultad de Ciencias, Universidad San Sebastián, Santiago, Chile, (4) Escuela de Nutrición y Dietética, Universidad San Sebastiá, (5) Facultad de Ciencias de la Salud y Ciencias Sociales, Universidad de las Américas, (6) Facultad de ciencias para el cuidado de la salud, Universidad San Sebastian, (7) Escuela de Tecnología Médica, Facultad de Ciencias, Universidad San Sebastián

Background/aims:

Gestational weight gain (GWG) outside recommended ranges is linked to maternal-infant outcomes. Because diet is a modifiable determinant of GWG, understanding the barriers that shape food-choice decisions is essential for designing counselling strategies in primary care.

Methods:

We analysed online questionnaire data from 66 pregnant women in the mami-educ randomised trial (ClinicalTrials.gov NCT05114174). Women indicated whether six barriers—price, access, taste, knowledge of use, knowledge of effects, medical indication—influenced their intent to raise fruit/vegetable intake or cut water, sugar, or salt. Responses were stratified by gestational-weight-gain (GWG) status: adequate (aGWG), excessive (eGWG) or insufficient (iGWG). Percentages denote the share of women selecting each barrier; multiple choices were allowed.

Results:

Across all GWG strata, personal taste was the dominant barrier (aGWG 61-98 %; eGWG 58-100 %; iGWG 75-100 %). In aGWG, personal taste deterred increased fruit (98 %) and water (98 %) intake, whereas medical indication strongly motivated reductions in sugar and salt (85 %). In eGWG, price was the leading obstacle to higher fruit (58 %) and vegetable (72 %) consumption, and knowledge of negative effects (58 %) figured prominently in sugar- and salt-related decisions. In iGWG, the combination of personal taste (>75 % for all foods) and high produce prices (fruit 83 %, vegetables 72 %) was most influential; knowledge of negative effects modulated choices around sugar (49 %) and salt (49 %).

Conclusions:

Although taste consistently limits healthy dietary changes during pregnancy, economic barriers arise among women with suboptimal GWG, while risk-related knowledge and medical advice influence sugar and salt decisions. Tailoring prenatal interventions to emphasize low-cost choices and reinforce the health risks of sodium and added sugars improves weight-management counseling in care centers.

Funding:

Institute of Public Policies of the San Sebastian University (IPSUSS1909); Agencia Nacional de Investigación y Desarrollo (ANID), FONDEF/XVIII Concurso Nacional de Proyectos de Investigación y Desarrollo en Salud, Fondo Nacional de Investigación y Desarrollo en Salud (FONIS)-7698SA21I0099.

Key-words: (up to 5): Pregnancy gestational weight gain
dietary barriers facilitators primary prevention

Abstract #00006361 en

Integration of the Legal Framework for Innovation and Biomedical Engineering: Reflections and Proposals for Advances in Public Health

Public Health Policies Across the Life Cycle.

Macedo Guimaraes dos Santos Weslaine (1), Macedo Guimaraes dos Santos Weslaine (1), Macedo Guimaraes dos Santos Weslaine (1) (1)
Universidade de Brasilia

Background/aims:
This study analyzes how the Legal Framework for Innovation influences the development of health research at the University of Brasília (UnB), focusing on Biomedical Engineering. It evaluates the role of the Center for Technological Development (CDT) and the Dean of Research and Innovation (DPI) in conducting R&D projects and in transferring technology to the health sector. The study aims to understand the challenges and potential of universities as agents of technological and social transformation.

Methods:
This is a qualitative analysis based on a review of public policies, institutional data, and interviews with researchers and managers involved in R&D projects in Biomedical Engineering at UnB. The research identifies the main bottlenecks and proposes guidelines to overcome obstacles in the practical application of the Legal Framework for Innovation.

Results:
Three main challenges were identified: (1) bureaucratic barriers and low adherence of the private sector to partnerships with universities, (2) the existence of the so-called 'Valley of Death' between research and market application, and (3) the underrepresentation of Biomedical Engineering among supported projects. Proposed solutions include legislative flexibility for universities, expanded tax incentives, and the creation of specific funds for health innovation. Applicable examples for the Brazilian Unified Health System (SUS) include low-cost diagnostic technologies, rehabilitation equipment, and chronic disease monitoring solutions.

Conclusions:
Overcoming the challenges in integrating innovation and public health requires joint efforts from universities, the government, and the private sector. Strengthening Biomedical Engineering and the innovation ecosystem is essential for improving the SUS and expanding equitable access to healthcare in Brazil.

Funding:
Not applicable / Under review

Key-words: (up to 5):
Legal Framework for Innovation; Biomedical Engineering; SUS; Health Innovation; Public Policies

Abstract #00006388 en

Nursing Diary: Frequency and Duration of Breastfeeding in Relation to Infant Sex and Maternal Body Mass Index

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Rocha Ana Carolina Lavio (1), Castro Lucíola Sant´Anna de (2), Camargo Bárbara Tideman Sartorio (2), Vieira Érika Loureiro (2), Horta Bernardo Lessa (3), Torsoni Adriana Souza (4), Cervantes MacKenzie K (5), Ross Michael G (6), Desai Mina (6), Coca Kelly Pereira (2)
(1) Universidade Federal de São Paulo (UNIFESP), (2) Universidade Federal de São Paulo, (3) Universidade Federal de Pelotas, (4) Universidade Estadual de Campinas, (5) Lundquist Institute. Harbor-UCLA Medical Center, (6) University of California, Los Angeles, UCLA

Background/aims:
Maternal nutritional status can influence breastfeeding, and infant sex may further modulate feeding patterns due to differences in growth patterns. Limited evidence exists on how these factors interact. This study aimed to examine sex-based differences in breastfeeding behavior among infants of Brazilian mothers with varying pre-pregnancy BMI.

Methods:
Brazilian postpartum women who gave birth to full-term singleton infants, and were exclusively breastfeeding were enrolled based on prepregnancy BMI (normal weight 18.5-24.9; overweight ≥ 25; obese ≥ 30). Mothers were instructed to record their infant's breastfeeding sessions over a 24-hour period (6 a.m to 6 a.m), using a nursing diary pattern (time and frequency of breastfeeding). The study was approved by the UNIFESP Ethics committee protocol n. 6.090.095.

Results:
Among the 37 postpartum women (1 to 4 months postpartum), 43% were of normal weight, 24% overweight, and 33% obese. The sample included 23 boys (mean age: 77 days; SD ±22) and 14 girls (mean age: 65 days; SD ±25). The mean daily duration of breastfeeding was 207 minutes per day (95% CI 167 to 246) among boys and 234 minutes per day (95% CI 182 to 285) among girls (p=0.38). We did not observe any difference in total time breastfeeding according to the infant's sex and maternal pregestational BMI. However, girls born to obese mothers had a significantly higher mean number of breastfeeding sessions per day compared to boys (12 [95% IC 8 to 16] vs 9 times [95% IC 8 to 10] p=0.03).

Conclusions:
Sex-based differences in breastfeeding frequency were observed among infants of obese mothers, suggesting that maternal nutritional status and infant sex may influence early feeding patterns. Larger studies with diverse populations are needed to confirm these findings and better understand the impact of maternal nutritional status on breastfeeding patterns.

Funding:
NIH grant #R01HD099813

Key-words: (up to 5):
breastfeeding, weight gain, infant, obesity

Abstract #00006396 en

Intraperitoneal administration of metformin in neonatal Wistar rats exerts a protective effect against diet-induced obesity in adulthood.

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Fuzeti Candian Bianca (1), de Assis Oliveira Claudio Guilherme (1), Damin João Victor (1), Gonçalves de Almeida Guilherme Henrique (1), Kurunzi Nunes Danielle (1), Gonçales Barbosa Guilherme (1), Rodrigues Raposo Scarlett (1), Ferreira Barbosa Leticia (1), Malta Ananda (1), Jacinto Saavedra Lucas Paulo (1), Piovan Silvano (1), Lopes de Almeida Douglas (1), Doná Rodrigues Almeida Gustavo Henrique (2), de Freitas Mathias Paulo Cézar (1) (1) State University of Maringá, (2) University of São Paulo

Background/aims:
The period between preconception and early childhood is characterized by heightened epigenetic plasticity, rendering it particularly sensitive to environmental influences. Early-life insults during this window may result in persistent metabolic alterations that predispose individuals to chronic diseases, such as obesity. Previous studies have demonstrated that oral administration of metformin in neonatal rats exerts long-term protective effects against obesity induced by early overnutrition. In this context, the present study aimed to evaluate whether intraperitoneal administration of metformin during the neonatal period mitigates diet-induced obesity in adulthood.

Methods:
Eighty male Wistar rats were randomly assigned to four groups (n = 20/group): saline-normolipidic (SAL-NL), metformin-normolipidic (MET-NL), saline-hyperlipidic (SAL-HL), and metformin-hyperlipidic (MET-HL). From postnatal days 1 to 12, animals received daily intraperitoneal injections of saline (0.9% NaCl) or metformin (100 mg/kg). All groups were fed a normolipidic diet from days 21 to 60; thereafter, SAL-HL and MET-HL received a high-fat diet until day 90. ITT, ivGTT and fat depot analyses were conducted at the end of the experiment.

Results:
At day 90, SAL-HL animals exhibited significantly greater body weight than SAL-NL ($p<0.05$), while MET-HL animals showed reduced body weight compared to SAL-HL ($p<0.05$). Furthermore, MET-HL rats presented decreased retroperitoneal, epididymal, and mesenteric fat ($p<0.05$). During ITT, MET-HL and MET-NL groups demonstrated lower glycemia compared to SAL-HL ($p<0.05$). No significant differences were observed in ivGTT; however, glycemic values in metformin-treated groups approximated those of SAL-NL.

Conclusions:
These findings suggest that neonatal intraperitoneal administration of metformin confers a protective metabolic programming effect, attenuating the development of obesity and insulin resistance in response to a high-fat diet in adulthood.

Funding:
CAPES and CNPq

Key-words: (up to 5):

Metformin, programming, high fat diet, metabolism.

Abstract #00006405 en

Type 2 Diabetes Mellitus Induced by Perinatal High-Sucrose Diet Leads to More Severe Liver Damage Than Type 1 Diabetes Mellitus in Adult Rats

Impact of Early Life Exposures and Environmental Pollutants

Sanches Jonas (1), Amorim Maria (2), França Álefe (1), Carvalho Suena (1), Brito Camila (1), Flister Karla (1), França Lucas (1), Alencar Luciana (1), Paes Antonio Marcus (1), Pinto Bruno (1)
(1) Federal University of Maranhão (UFMA), (2) Federal University of Maranhão (UFMA)

Background/aims:
Nutritional challenges during critical developmental windows may have lifelong consequences for metabolic health. This study investigated the long-term hepatic morpho-functional effects of type 2 diabetes mellitus (DM), programmed by maternal high-sucrose intake, in comparison with type 1 DM induced in adulthood.

Methods:
Female Wistar rats were fed either standard chow (CTR; 10% sucrose) or a high-sucrose diet (HSD; 25% sucrose) from preconception through lactation. A separate group was rendered hypoinsulinemic at 12 weeks via a single streptozotocin injection (STZ, 65 mg/kg, i.p.). All male offspring (n=5/group) received standard chow after weaning and were evaluated at 24 weeks. Analyses included glucose metabolism, lipid profile, hepatic histology, gene expression, and hepatocyte nanomechanics via atomic force microscopy (AFM) (CEUA/UFMA 23115.000747/2022-90).

Results:
HSD offspring developed hyperinsulinemia ($p < 0.05$), mild hyperglycemia ($p < 0.05$), insulin resistance (↑HOMA, $p < 0.01$), and dyslipidemia (+95.5% triglycerides, $p < 0.05$). Liver analysis revealed microvesicular steatosis ($p < 0.0001$), parenchymal fibrosis, and increased gene expression of PPAR-γ, FASN, and DGAT. AFM revealed significant increases in hepatocyte volume, surface roughness, and stiffness (all $p < 0.0001$). In contrast, STZ-treated hypoinsulinemic rats presented severe hyperglycemia ($p < 0.0001$) and marked hypoinsulinemia ($p < 0.05$). Despite this intense metabolic disturbance, hepatic alterations were limited to mild perivascular fibrosis without steatosis, with no significant changes in lipogenic gene expression. However, AFM revealed increased hepatocyte adhesion forces ($p < 0.0001$), suggesting early biomechanical remodeling even in the absence of overt steatosis or widespread fibrosis.

Conclusions:
Exposure to a high-sucrose environment during the perinatal period programs persistent hepatic metabolic and biomechanical dysfunction, surpassing the impact of hypoinsulinemia acquired in adulthood. These findings underscore the critical role of early-life nutritional and hormonal environments in shaping long-term liver health and susceptibility to metabolic diseases.

Funding:
CNPq, CAPES and FAPEMA.

Developmental programming; Hyperinsulinemia; Hypoinsulinemia; Liver dysfunction.

Key-words: (up to 5):

Abstract #00006418 en

The impact of maternal hyperglycemia on the liver-brain axis in offspring: A rodent model of overt diabetes

Mechanisms Determining Transgenerational Effects of Health and Disease

Rodrigues Nathalia Késsia Corrêa (1), Melo Thamys Marinho (1), Sousa Nayra Oliveira (1), Santos Jefferson Oliveira De Almeida (1), Oliveira Luiza De Katulica Rodrigues (1), Alencar Maysa Souza de (1), Sanches Jonas Rodrigues (1), Flister Karla Frida Torres (1), Paes Antônio Marcus de Andrade (1), Pinto Bruno Araújo Serra (1) (1) Federal University of Maranhão (UFMA)

Background/aims:
Overt diabetes (OD) during pregnancy is a significant public health concern, associated with adverse short- and long-term outcomes in offspring, including metabolic syndrome, type 2 diabetes (T2D), non-alcoholic fatty liver disease (NAFLD), and cognitive impairments. This study investigated whether maternal OD programs systemic, hepatic, and neurobehavioral dysfunctions in adult offspring via early-life exposure to hyperglycemia.

Methods:
Pregnant Wistar rats were assigned to control (CTR; n=6) or OD (n=10) groups, with OD induced by a single intraperitoneal injection of streptozotocin (40 mg/kg) on gestational day 13. Offspring were divided into three groups: CTR, OD, and T2D (DM2; induced by 40% sucrose from week 6). At 18 weeks, we assessed body morphometry, glucose and lipid profiles, insulin resistance (TyG index), liver function (ALT, AST, histopathology), and cognitive behavior (open field, object recognition, and water maze tests).

Results:
STZ-treated dams exhibited severe hyperglycemia, insulin resistance, and weight loss. OD offspring presented reduced birth weight, neonatal hyperglycemia, and persistent metabolic alterations in adulthood, including hyperglycemia, dyslipidemia, and NAFLD with microvesicular steatosis, lobular inflammation, and hepatocellular ballooning. Notably, OD animals showed cognitive deficits and anxiety-like behavior, even in the absence of obesity, indicating a direct effect of early hyperglycemia on neurodevelopment. Although DM2 rats showed more pronounced insulin resistance and visceral obesity, their liver damage was milder and behavioral deficits similar to the OD group.

Conclusions:
These results highlight that maternal OD acts as an early-life metabolic disruptor, triggering long-lasting alterations in glucose homeostasis, liver health, and cognitive function. The findings underscore the relevance of the liver-brain axis as a target of developmental programming by maternal diabetes and emphasize the urgent need for early prevention and management of OD to reduce long-term chronic disease risk in the next generation.

Funding:
CNPq, CAPES and FAPEMA

Developmental programming; Overt diabetes; Non-alcoholic fatty liver disease (NAFLD); Cognitive impairment.

Abstract #00006438 en

Mental health during pregnancy and neonatal anthropometric outcomes: Results from the OBESO Cohort

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Suarez-Rico Blanca (1), Mendoza-Ortega Jonatan Alejandro (2), Osorio Valencia Erika (3), Hernández Chávez Carmen (3), Gil Martínez Gabriela (3), Rodríguez-Hernández Carolina (1), Perichart Pereira Otilia (1), Rodríguez Cano Ameyalli (1), González Ludlow Isabel (1), Reyes Muñoz Enrique (4), Estrada Gutiérrez Guadalupe (2)

(1) Department of Nutrition and Bioprogramming, INPer, (2) Department of Immunobiochemistry, INPer, (3) Department of Developmental Neurobiology, INPer, (4) Endocrinolgy Coordination, INPer

Background/aims:

Maternal psychosocial factors during pregnancy are key determinants of offspring health. This study assessed the independent correlation between maternal mental health during pregnancy (stress, anxiety, and depression) and neonatal anthropometric outcomes in a Mexican birth cohort.

Methods:

Data were obtained from participants in the Epigenetic and Biochemical Origin of Overweight and Obesity (OBESO) prospective cohort study. Inclusion criteria included: singleton pregnancy, enrollment before 14 weeks of gestation, absence of chronic diseases (e.g., diabetes, hypertension), and availability of maternal and neonatal data. Maternal mental health was evaluated using validated psychometric scales during the second trimester: perceived stress (PSS-4), depression (Edinburgh Postnatal Depression Scale), and anxiety (IDARE). Neonatal anthropometric assessments were performed within 24–48 hours after birth and included birth weight, length, head circumference, and abdominal circumference. Correlation and regression analyses were conducted. All participants provided informed consent (IRB 3300-11402-01-575-17//2024-1-14).

Results:

Data from 218 mother-infant pairs were analyzed. The mean (SD) scores for maternal mental health were: stress – data pending, anxiety trait – 36.76 (10.62), anxiety state – 34.61 (10.28), and depression – 7.25 (6.10). The mean (SD) gestational age at birth, birth weight, and head circumference were: 38.8 (2.2) weeks, 3.02 (0.47) kg, and 33.30 (1.43) cm, respectively. A higher maternal anxiety state score during pregnancy had a significantly correlation with a smaller neonatal head circumference ($r = –0.18$, $p = 0.01$). No significant correlations were observed between maternal perceived stress, anxiety trait, or depression and other neonatal anthropometric outcomes.

Conclusions:

High maternal score in anxiety state during pregnancy is negatively correlated with neonatal head circumference size, a marker of early brain growth. These findings underscore the importance of identifying and addressing maternal mental health as part of prenatal care to support optimal fetal neurodevelopment.

Funding:

Instituto Nacional de Perinatología (No. 3300-11402-01-575-17/2024-1-14).

Key-words: (up to 5):

Maternal mental health
Anxiety
Neonatal anthropometry
Head circumference
Pregnancy

Abstract #00006449 en

Impact of obesity on haemoglobin levels in obese postpartum women

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Wolf Lebrão Cibele (1), Giovanelli Silvana (1), Vivi Anna Caroline (2), Silva Aldrin (3), Pereira-Leite Narjara (3), Suano de Souza Fabiola Isabel (4)
(1) Hospital da Mulher de São Bernardo do Campo, (2) UNIFESP, (3) FMABC, (4) Universidade Federal de São Paulo

Background/aims:
Anaemia is prevalent among pregnant women; however, few studies have evaluated haemoglobin levels in the immediate postpartum period, which may increase the risk of complications and compromise lactation. This study aimed to assess haemoglobin levels in postpartum women and correlate them with maternal nutritional status and weight gain during pregnancy.

Methods:
A cross-sectional, controlled study with 66 postpartum women (30 eutrophic and 66 obese according to pre-pregnancy body mass index). Data collected: weight gain during pregnancy, maternal diseases, physical activity level, newborn anthropometry at birth, complete blood count, and maternal C-reactive protein levels collected up to 48 hours after delivery.

Results:
Women in the pre-pregnancy obesity group were older (29.45 ± 4.09 kg/m² vs. 25.57 ± 5.07 kg/m², p = 0.004). Hypertensive disease was more prevalent in the group with pre-gestational obesity (20.0% vs. 2.2%, p = 0.027). The percentage of postpartum women with anaemia (Hb < 10 g/dL) in the postpartum period was 18.2%, with no difference between the groups. In the bivariate analysis, the MCV (86.25±7.31 fl vs. 89.43±4.16 fl, p = 0.028) and MCH (29.55±2.74 pg vs. 30.89±1.91 pg, p = 0.026) values were lower in the group with pregestational obesity. This association remained after adjustment for maternal age and ethnicity for MCV (β = -3.359, 95% CI -6.62 to -0.97, p = 0.044) and MCH (β = -1.473, 95% CI -2.82 to -0.12, p = 0.033).

Conclusions:
The frequency of anaemia was not higher in the group with pre-gestational obesity; however, MCV and MCH values were lower in this group, indicating that adequate maternal nutritional status, in combination with iron supplementation, may influence the risk of anaemia during pregnancy and the postpartum period.

Funding: NA

Key-words: (up to 5):
postpartum, anaemia, obesity

Abstract #00006482 en

Surgical Site Infection Prevention for Improving Quality of Care

Public Health Policies Across the Life Cycle.

Bilal Muhammad (1), Sadia Afreen (1), Saleem Sarah (1), Sadiq Hassaan (1), Ahmed Imran (1), Irfan Seema (1), Zafar Afia (1)
(1) The Aga Khan University

Background/aims:

Methods:

Results:

Conclusions:

Funding:

Key-words: (up to 5):

Abstract #00006664 en

Female cortical cellular mosaicism underlies shared MeCP2 and PCB impacted gene pathways

Big Data and Cohorts in DOHaD Research.

Sharifi Osman (1)
(1) University of California, Davis

Background/aims:
Rett Syndrome (RTT) is an X-linked neurodevelopmental disorder caused by MECP2 mutations, creating cellular mosaicism in females due to random X-chromosome inactivation. Variable RTT progression suggests environmental factors like polychlorinated biphenyls (PCBs) may interact with genetic mutations. We used single-nucleus RNA sequencing on cortical cells from adult female mice exposed to a MARBLES study-derived PCB mixture to investigate gene-environment interactions.

Methods:
We crossed Mecp2e1-/+ females with wild-type males, exposing ~10-week-old females to 0.01 mg/kg/day PCB mixture or vehicle control for 6 weeks (4 mice/group). At ~16 weeks, we harvested cortices and processed 150,000 nuclei per sample using flow sorting and 10× Genomics single-cell 5' RNA sequencing. We performed differential expression analysis using LimmaVoom across 15 comparisons and parsed Mecp2e1 alleles to distinguish wild-type from mutant cells in mosaic brains.

Results:
We identified 12 cortical cell types and found PCB exposure normalized some transcriptional disruptions in RTT mice, with fewer dysregulated genes in PCB-treated mutants. Analysis revealed 71 overlapping dysregulated pathways affecting synaptic functions. PCB exposure predominantly affected wild-type-expressing neurons rather than mutant cells. Cross-species validation with human RTT cortex showed conserved responses, with GABAergic neurons showing greatest overlap (7,931 shared genes).
Oxytocin signaling was the only pathway commonly affected across all cell types in both species.

Conclusions:
PCB exposure mitigates RTT-related gene dysregulation, primarily impacting wild-type neurons in mosaic brains. GABAergic neurons, particularly Sst cells, showed strongest PCB-Mecp2 interactions, with Xist gene involvement. These findings reveal conserved molecular mechanisms and could inform therapeutic strategies targeting excitatory/inhibitory balance disruptions.

Funding:
NIH T32ES007059, R01ES029213, R01AA027075, S10OD010786, U2CES030158, and U24DK097154.

Key-words: (up to 5):
neurodevelopmental disorders, persistent organic pollutants, polychlorinated biphenyls, Rett syndrome, X chromosome inactivation

Abstract #00006665 en

Gestational Protein Restriction Induces an Osteoporosis-Like Phenotype in Aging Offspring

Impact of Early Life Exposures and Environmental Pollutants

Calsa Bruno (1), Breanza Giovani Vinhato (2), Melo Renata Marinho (2), Gontijo José Antonio Rocha (1), Santamaria-Jr Milton (2), Boer Patrícia Aline (1)
(1) Faculty Medical Science, State University of Campinas - UNICAMP, (2) Institute of Science and Technology, College of Dentistry - UNESP

Background/aims:
Osteoporosis is characterized by low bone mineral density, deterioration of bone microarchitecture, and increased bone fragility. However, no studies have evaluated bone physiology in aged animals exposed to gestational low-protein diet, leaving a gap in understanding how early-life undernutrition affects skeletal health during aging.

Methods:
This study was approved by the Ethics Committee (5923-1/2021). Female C57BL/6J mice were mated and randomly assigned to two groups during gestation: normal protein (NP, 17% casein) or low protein (LP, 6% casein). After birth, all dams and pups were fed with a standard diet. Femurs from male offspring were collected at 12 and 18 months of age. Micro-computed tomography was performed to assess bone parameters in the femoral distal metaphysis and diaphysis. A three-point bending test was conducted to evaluate bone strength. Additionally, scanning electron microscopy (SEM) fractography was performed to analyze ultrastructural features, and femoral RNA sequencing was carried out.

Results:
Gestational protein restriction led to a reduction in trabecular bone fraction, bone mineral density, and trabecular number at 18 months, and decreased cortical thickness at both 12 and 18 months. LP-18M mice exhibited significantly reduced maximal load, indicating compromised bone strength. Ultrastructural analysis revealed increased surface porosity in LP-18M bones. A reduction in collagen fibers was observed in bone matrix in LP-18M animals. RNA-seq identified 125 differentially expressed genes, with enrichment in pathways related to macrophage migration and osteoclast differentiation. RT-qPCR validation confirmed increased inflammatory signaling and osteoclast activation through genes such as Ccl3, Ccr2, Junb, Lilrb4a, and Trem2.

Conclusions:
Maternal protein malnutrition significantly impairs trabecular and cortical bone, leading to reduced bone mass, mineral density, and mechanical strength. The transcriptomic profile indicates enhanced osteoclast activation in LP animals. These findings suggest that gestational protein restriction contributes to bone loss and predispose offspring to osteoporosis-like phenotype in later-life.

Funding:
São Paulo Research Foundation - FAPESP, Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – CAPES

Key-words: (up to 5):
Osteoporosis, undernutrition, bone.

Abstract #00006671 en

Effects of Gestational Protein Restriction on Liver Development in Male Mice at Embryonic Day 14

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Lopes Marcelo Gustavo (1), Folguieri Marina Silva (2), Calsa Bruno (2), Gomes Julia Seva (2), Boer Patricia Aline (2), Gontijo Jose Antonio Rocha (2)
(1) State University of Campinas (UNICAMP), (2) State University of Campinas

Background/aims:
Fetal programming refers to the way adverse intrauterine conditions, such as maternal protein restriction, can influence organ development and increase the risk of disease in offspring. The liver, a metabolically and hematopoietically active organ during embryogenesis, is susceptible to such influences. This study aimed to assess the effects of gestational protein restriction on hepatic development in male mouse embryos at embryonic day 14 (E14).

Methods:
C57BL/6J and transgenic CAG-RFP-EGFP-LC3 mice (autophagy LC3 marker) were mated and divided into two groups: normal protein (NP; 17% casein) and low protein (LP; 6% casein) diets during gestation. Embryos were collected at E14 for assessment of anthropometric data, hepatic proliferation, autophagy, and expression of growth factor genes (PCR array).

Results:
LP embryos exhibited reduced fetal weight, placental weight, and increased placenta-to-fetus ratio ($p<0.05$). LP livers presented a 62% reduction in LC3-positive autophagic vesicles ($p=0.015$). Gene profiling showed upregulation of 17 growth-related genes in LP embryos, notably Gdnf (172-fold), Bmp4, Fgf10, and Mdk. Immunohistochemical staining of ERK1/2 and NF-κB revealed increased expression in LP embryos, supporting the transcriptomic alterations and confirming our findings from the PCR array. Autophagic vesicles were quantified using confocal microscopy, and gene expression was considered relevant with fold change ≥2 and $p<0.05$.

Conclusions:
Gestational protein restriction induces early hepatic alterations marked by reduced autophagy and significant upregulation of growth factor genes. These findings suggest adaptive responses aimed at preserving liver growth and function but may predispose to long-term metabolic or inflammatory dysregulation.

Funding:
FAPESP/CNPq/CAPES

Key-words: (up to 5):
Fetal programming, Liver development, Protein restriction, Autophagy, Growth factors

Abstract #00006674 en

Dexamethasone is associated with Ductal Closure in Extremely Preterm Infants with Evolving Lung Disease

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Plessas-Azurduy Phoenix (1), Hazan Mea Joshua (2), Sonea Thomas (3), Kanaprach Pasinee (4), Michel Macías Carolina (5), Sara Moore Shiran (6), Wutthigate Punnanee (7), Simoneau Jessica (2), Villegas Martinez Daniela (2), Villeneuve Andréanne (8), Lapointe Anie (8), Sant'Anna Guilherme (2), Altit Gabriel (2)

(1) Division of Clinical and Translational Research, McGill University, (2) Division of Neonatology, McGill University, (3) Faculté de médecine, Université de Montréal, (4) Division of Neonatology, Department of Pediatrics, Montreal Children's Hospital, (5) Universidad Autónoma de Querétaro, Facultad de Medicina, (6) Division of Neonatology, Department of Pediatrics, Dana Dwek Children's Hospital, (7) Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, (8) Division of Neonatology, CHU Sainte-Justine, Université de Montréal

Background/aims:

Dexamethasone (DEXA) is administered to premature neonates with evolving lung disease, often on mechanical ventilation. Extremely premature infants frequently have a patent ductus arteriosus (PDA), associated with bronchopulmonary dysplasia (BPD). While DEXA is widely used to prevent and treat BPD, its impact on PDA closure remains unclear. This study evaluated changes in PDA size and closure rates following DEXA administration in a population exposed to a conservative PDA management policy, hypothesizing that DEXA treatment is associated with PDA size reduction and closure.

Methods:

This prospective observational cohort study included preterm neonates (<29 weeks gestational age [GA]) receiving DEXA for evolving BPD. Serial echocardiography was performed at seven timepoints: baseline, days 3, 7, and 14 of treatment, 1 and 2 weeks post-treatment, and 36 weeks corrected GA. PDA size was measured by a blinded evaluator.

Results:

From 2021–2024, 52 neonates were recruited (61% male, 79% inborn). Mean birth GA was 25.4 weeks (SD: 1.4) and mean birthweight was 757 g (SD: 192 g). Median APGAR scores were 6 and 8 at 5 and 10 minutes. The GEE model showed a significant increase in PDA closure likelihood over time (coefficient: 0.47, $p < 0.001$). PDA size decreased by 0.21 mm per timepoint ($p < 0.001$), from 2.02 ± 0.70 mm to 1.44 ± 0.64 mm by timepoint 7. By 36 weeks, 97% of infants had complete closure or a restrictive PDA.

Conclusions:

DEXA treatment was associated with a temporal reduction in PDA size and patency, suggesting additional benefits beyond its pulmonary effects.

Funding:

Gabriel Altit is a Clinician Scholar Junior 1 from the FRQS. The SPEC study was partly funded by the Pediatric Research Foundation, New Direction Grant from the Department of Pediatrics of McGill University, and the Just for Kids Foundation.

Phoenix Plessas-Azurduy's graduate work was partly funded by the McCall MacBain Finalist Scholarship awarded by McGill University and the Graduate Excellence Award from the Division of Clinical & Translational Research at McGill University.

Key-words: (up to 5):
Extremely Preterm Infants, Patent Ductus Arteriosus (PDA), Bronchopulmonary Dysplasia (BPD), Postnatal steroids, Echocardiography

Abstract #00006682 en

In Breastfeeding Women, Pregestational Obesity Results in Excessive Infant Weight Gain through Six Months of Age

Role of Infant and Young Child Feeding Practices on Long-Term Health

de Castro Luciola Sant Anna (1), Rocha Ana Carolina Lavio (1), Camargo Bárbara Tideman Sartorio (1), Horta Bernardo Lessa (2), Torsoni Adriana Souza (3), Ross Michael G (4), Desai Mina (4), Coca Kelly Pereira (1)
(1) Federal University of Sao Paulo, (2) Federal University of Pelotas, (3) State University of Campinas, (4) University of California

Background/aims:
Rapid weight gain in infancy is associated with future health risks, including childhood and adult obesity. It remains controversial whether breastfeeding reduces the risk of excessive infant weight gain. As the milk of obese women has increased fat and caloric content, compared to normal weight women, we sought to assess the association of maternal pregestational BMI with growth trajectories of exclusively breastfed infants.

Methods:
Postpartum women at a breastfeeding center in São Paulo, Brazil with full-term, singleton infants were enrolled and followed from the first to the sixth month postpartum. Participants were grouped according to their pregestational BMI: normal weight (n=54; 18.5–24.9 kg/m²), overweight (n=42; 25.0–29.9 kg/m²), and obese (n=20; ≥ 30.0 kg/m²). Infant weight and length were measured monthly and sex-specific anthropometric indices—BMI-for-age, weight-for-age, and height-for-age—based on the growth standards established by the World Health Organization were estimated. The study was approved by the Ethics Committee of UNIFESP, São Paulo, Brazil, under protocol number 4.067.970. Z-scores were compared among the BMI groups with infants of normal weight women set at reference 0.

Results:
Infants born to obese mothers showed a higher change in BMI-for-age z-score (mean difference: 0.82; 95% CI: 0.25 to 1.39) and weight-for-age z-score (mean difference: 0.64; 95% CI: 0.13 to 1.16) compared to those born to normal weight mothers at six month age. No significant difference was observed in the height-for-age z-score between the groups (mean difference: 0.06; 95% CI: –0.40 to 0.53).

Conclusions:
Maternal obesity was associated with excessive infant weight gain during the first six months of life, despite exclusive breastfeeding. Together with prior studies, these results suggest that increased breast milk caloric content promotes infant weight gain. Novel interventions to prevent excessive infant weight gain, particularly in obese mothers are necessary to interrupt generational obesity.

Funding:
This research was funded by the Coordination for the Improvement of Higher Education Personnel - Brazil (CAPES).

Key-words: (up to 5):
breastfeeding, infant growth, nutritional status, obesity

Abstract #00006684 en

The impact of prenatal factors on childhood growth trajectories – findings from the LIMIT randomised trial and childhood follow-up.

Impact of Early Life Exposures and Environmental Pollutants

Dodd Jodie M (1), Deussen Andrea R (1), Louise Jennie (2), Mitchell Megan (1)
(1) University of Adelaide, Adelaide, (2) South Australian Health and Medical Research Institute, Adelaide

Background/aims:
Obesity continues to represent a significant public health issue with The First 1,000 Days of Life identified as a potentially critical period in the development of child obesity. Our aim was to evaluate the relationship between maternal, paternal and pregnancy factors with childhood growth trajectories.

Methods:
We utilised the LIMIT RCT cohort of women with overweight and obesity who were randomised to receive standard care, or a dietary and lifestyle intervention in pregnancy. Pregnancy outcomes included early pregnancy body mass index (BMI), gestational diabetes (GDM), gestational weight gain (GWG) and infant birth weight, as well as paternal BMI. Children underwent follow-up assessments at 6 months, 18 months, 3-5 years and 8-10 years of age, including measurement of weight, BMI, and z-scores for each. Linear mixed models were used to estimate the effect of the pregnancy intervention at each child timepoint for each outcome and estimated the direct effect of early life variables on child growth trajectory.
Ethics approval was provided by the Women's and Children's Hospital Human Research and Ethics Committee.

Results:
We identified no evidence of discrete child growth trajectory patterns, or of an effect from providing an antenatal dietary intervention. Increasing maternal BMI, paternal BMI and infant birth weight were all significantly associated with increases in childhood growth trajectories for child BMI, child weight and both BMI and weight z-scores. We did not identify an impact from either GWG or a diagnosis of GDM on child growth trajectories.

Conclusions:
The relationships identified between maternal early pregnancy BMI and paternal BMI on subsequent childhood growth, highlight the need to support women and their partner to optimise health, including BMI, prior to conception.

Funding:
NHMRC Project Grants (APPS 519240; 1043178; 1068320; 1159338); NHMRC Investigator Grant (APP1196133)(JMD).

Key-words: (up to 5):
Randomised trial; preconception health; pregnancy; childhood growth

Abstract #00006685 en

Causal relationships between maternal BMI, gestational weight gain, and adverse pregnancy outcomes.

Mechanisms Determining Transgenerational Effects of Health and Disease

Dodd Jodie M (1), Louise Jennie (2), Deussen Andrea R (1), Mitchell Megan (1), Poston Lucilla (3)
(1) University of Adelaide, Adelaide, (2) South Australian Health and Medical Research Institute, Adelaide, (3) King's College, London

Background/aims:
Our aim was to evaluate commonly assumed causal relationships between maternal body mass index (BMI), gestational weight gain (GWG) and adverse pregnancy outcomes, which have formed the basis of pregnancy guidelines and interventions directed at limiting GWG in women with overweight or obesity, and a strategy attempting to break the intergenerational cycle of obesity. We explored relationships between maternal BMI, total GWG (as a continuous variable, and as “excessive” GWG), and pregnancy outcomes (including infant birthweight measures and caesarean birth).

Methods:
We utilised individual participant data from the i-WIP (International Weight Management in Pregnancy) Collaboration, from randomised trials of diet and/or physical activity interventions during pregnancy, where GWG and maternal and neonatal outcomes were reported. We included data from 4,370 participants in the control group of 20 international RCTs. We characterised the relationship between maternal BMI and total GWG; the risk of “excessive” GWG; and the extent to which adverse pregnancy outcomes were mediated via GWG or other pathways. We used generalised linear models and regression-based mediation analyses within an IPD Meta-Analysis framework.

Results:
While mean GWG decreased linearly as maternal BMI increased, the risk of “excessive” GWG increased at the BMI category thresholds. Increasing maternal BMI was associated with increased risk of all pregnancy outcomes assessed, however, there was no evidence that this effect was mediated via effects on GWG.

Conclusions:
We identified evidence of a meaningful relationship between maternal BMI and GWG, and between maternal BMI and adverse pregnancy outcomes. However, we did not identify evidence to indicate that the effect of maternal BMI on pregnancy outcomes was via an effect on GWG.

Funding:
NHMRC Investigator Grant (JMD) (APP1196133).

Key-words: (up to 5):
Gestational weight gain; pregnancy; dietary and lifestyle intervention; causal pathways; body mass index

Abstract #00006686 en

The impact of maternal BMI and antenatal dietary intervention during pregnancy on cord blood epigenetics – findings from the LIMIT, GRoW and OPTIMISE randomised trials.

Mechanisms Determining Transgenerational Effects of Health and Disease

Mitchell Megan (1), Deussen Andrea R (2), Louise Jennie (3), Dodd Jodie M (2)
(1) University of Adelaide, (2) University of Adelaide, Adelaide, (3) South Australian Health and Medical Research Institute, Adelaide

Background/aims:
Obesity represents a significant public health issue with many inter-related early life exposures potentially contributing to the development of child obesity. Epigenetic modification has been postulated as mechanism on the pathway to child obesity.
Our aims were to evaluate whether there was evidence of epigenetic modification:
1) following provision of a maternal dietary and lifestyle intervention during pregnancy; and 2) attributable to maternal body mass index (BMI) in early gestation.

Methods:
We utilised our harmonised suite of randomised controlled trials in which women were randomised to a comprehensive dietary intervention across pregnancy or to standard antenatal care. Women participated in the LIMIT RCT (BMI >25.0kg/m2); the GRoW RCT (BMI >25.0kg/m2 who received metformin or placebo as an adjuvant therapy); or the OPTIMISE RCT (BMI <25.0kg/m2). We measured DNA methylation in neonatal cord blood samples from participants using the Illumina Infinium Human Methylation 850K (EPIC) Bead-Chip array. We tested for any differential methylation related to the intervention, or to maternal early pregnancy BMI. We also analysed differential methylation in relation to selected candidate genes.

Results:
We examined 535 samples from LIMIT; 262 samples from GRoW; and 293 samples from OPTIMISE. We did not identify any CpG sites that were significantly differentially methylated in relation to either the diet and lifestyle intervention, or with maternal early pregnancy BMI. There was no significant differential methylation in any of the selected genes related to the intervention, or to maternal BMI.

Conclusions:
We found no evidence of an effect of either antenatal diet and lifestyle, or of maternal early pregnancy BMI, on neonatal DNA methylation.

Funding:
NHMRC Project Grants (APPS 519240; 1043178; 1068320; 1159338; 1043181); NHMRC Investigator Grant (JMD) (APP1196133).

Key-words: (up to 5):
Randomised trial; pregnancy; epigenetics

Abstract #00006687 en

Effects of intrauterine exposure to nicotine on sex hormones and ovarian follicular reserve of adult rats

Impact of Early Life Exposures and Environmental Pollutants

dos Santos Isabela Dinis (1), Reis Isabella de Lima (1), da Costa Samuel Rebouças (1), de Vasconcelos Katia (1), Gil Cristiane Damas (1), Paccola Camila Cicconi (1)
(1) Federal University of Sao Paulo

Background/aims:
Smoking can cause irregular reproductive cycles, early menopause, decreased fertility, and reproductive problems in smokers' descendants. The main component of cigarettes is nicotine, also found in cigars, e-cigarettes and nicotine-replacements (gums and patches). Maternal nicotine-exposure can affect preand postnatal development, altering gonadal development, puberty onset and hormonal control of males and females, raising discussions related to the Developmental Origins of Health and Disease. Furthermore, nicotine has a "dual" effect on hormonal and proliferation/death cellular control, stimulating or reducing apoptosis (leading to cancer). Thus, we aimed to verify the effects of the intrauterine and lactational nicotine-exposure on the hormones of the hypothalamic-pituitary-gonadal axis and ovarian follicular reserve of adult rats.

Methods:
After Ethics Committee for Animal Use (CEUA-UNIFESP) approval, ten rats received an osmotic pump containing nicotine (2 mg/kg/day) from the first gestational-day until the end of breastfeeding. Ten control rats received minipumps without nicotine. When the offspring reached 90 days of age, one female/litter had blood and ovaries collected. Serum levels of GnRH, FSH, LH, estradiol, progesterone and AMH were measured. In the ovaries were analysed the oocyte (MVH-labeled) number, protein expression of cell proliferation (PCNA) and death (cleaved Caspase-3) and FSH- and LH-receptors, by Western blotting.

Results:
No changes were found in oocyte number, cell proliferation and death proteins or rLH in the ovaries of exposed offspring. GnRH, FSH, progesterone and AMH were also unchanged. On the other hand, serum estradiol and LH and ovarian rFSH were significantly reduced in exposed animals.

Conclusions:
Although intrauterine and lactational exposure to nicotine does not affect ovarian follicular reserve, it affects the sex hormones in adulthood. These data reinforce the need to raise awareness among the population about the risks of nicotine consumption in any form (including e-cigarettes, increasingly consumed by young people), especially during pregnancy.

Funding:
São Paulo Research Foundation (FAPESP) #2024/01377-5 and #2024/02422-4

Key-words: (up to 5):
Nicotine; female reproduction; sex hormones, ovary; rats

Abstract #00006690 en

The impact of maternal vitamin D concentrations on fetal adiposity and growth: longitudinal evidence from the Araraquara Cohort Study.

Public Health Policies Across the Life Cycle.

Oliveira Aires Isabel (1), Victor Audencio (1), Ramos Silva Tamiris (1), Antonia Martins Rodrigues Francilany (1), Sampaio Praxedes Giovanna (1), Pinheiro-Castro Natália (1), Alves Luzia Liania (1), Helen de Carvalho Rondó Patrícia
(1)
(1) School of Public Health (University of São Paulo)

Background/aims:
Vitamin D [25(OH)D] plays a key role in fetal development during pregnancy. However, its influence on fetal growth and adiposity remains unclear, demanding studies that explore this relationship in a longitudinal way, particularly in relation to adiposity. The present study aimed to evaluate the association between maternal 25(OH)D concentrations and fetal growth and adiposity throughout pregnancy.

Methods:
Data from 330 pregnant women enrolled in the Araraquara Cohort Study in São Paulo, Brazil [Ethics Committee: 67483517.6.0000.5421]. Serum 25(OH)D concentrations were measured during three gestational periods (< 19; 20–28 and 30–36 weeks). Fetal outcomes included ultrasound measurements of growth (estimated fetal weight, femur length, abdominal, head circumference, and biparietal diameter) and adiposity (subcutaneous and muscle areas of the thigh and arm). Generalised estimating equation models with an autoregressive correlation structure were used to assess associations throughout pregnancy, adjusting for maternal age, education, parity, pre-pregnancy Body Mass Index, gestational weight gain, income, smoking, alcohol consumption, nutritional supplement, and pregnancy complications.

Results:
In crude models, higher maternal 25(OH)D was associated with increased femur length ($\beta = 0.0105$; $p < 0.001$), abdominal circumference ($\beta = 0.0427$; $p = 0.001$), head circumference ($\beta = 0.0533$; $p < 0.001$), biparietal diameter ($\beta = 0.0116$; $p = 0.001$), estimated fetal weight ($\beta = 5.91$g; $p < 0.001$), total thigh area ($\beta = 0.0224$; $p = 0.010$), thigh muscle area ($\beta = 0.0126$; $p = 0.009$), thigh fat area ($\beta = 0.0092$; $p = 0.026$), and arm muscle area ($\beta = 0.0051$; $p = 0.024$). After adjustment, only head circumference remained marginally associated ($\beta = 0.0043$; $p = 0.049$) with maternal 25(OH)D.

Conclusions:
In this study, maternal 25(OH)D concentrations were positively associated with fetal head circumference, but were not associated with other fetal growth and adiposity parameters. Potential effects on fetal adiposity warrant further exploration.

Funding:
Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) – grant numbers: 2015/03333-6 and 2024/01014-0.

Key-words: (up to 5):
Vitamin D, fetal growth, fetal adiposity, ultrasound, pregnancy

Abstract #00006695 en

Lasting impact of maternal depressive symptoms on child cognitive and mental health outcomes in middle-childhood: Evidence from an urban poor cohort in South India

Impact of Early Life Exposures and Environmental Pollutants

Lobo Eunice (1), Ravi Deepa (1), Karande Akanksha B (1), Srinivas Prashanth Nuggehalli (1), CP van Schayck Onno (2), Rathnaiah Babu Giridhara (3), Mukherjee Debarati (4)
(1) Indian Institute of Public Health - Bengaluru, Public Health Foundation of India, (2) Care and Public Health Research Institute (CAPHRI), Maastricht University, (3) Department of Population Medicine, College of Medicine, QU Health, Qatar University, (4) Centre for Developmental and Lifecourse Research, Public Health Foundation of India

Background/aims:
Maternal mental health during the perinatal period critically impacts child development, yet its long-term effects in the Global South are understudied. The COINCIDE study examines associations between maternal depressive symptoms in the first 1000 days with cognitive and mental health outcome of 4-6-year-old children in urban poor households in Bangalore, India

Methods:
We used prospective data from 352 mother-child dyads recruited from the MAASTHI birth cohort and followed up through the COINCIDE study. Maternal depressive symptoms were assessed using the Edinburgh Postnatal Depression Scale (EPDS) at pregnancy, 1 year, 2 years, and when children were aged 4-6-years. Children's non-verbal logical reasoning abilities (measured using the Raven's Coloured Progressive Matrices [RCPM]) and internalizing and externalizing behaviours (measured using the Strengths and Difficulties Questionnaire [SDQ]) were assessed when children were 4-6-years old.
Confounder adjusted linear regression modelling and cluster analysis were used to examine associations.

Results:
Maternal depressive symptoms during the pregnancy, and post-partum period (when children were 1 year, and 4-6-years old) were positively associated with internalizing behaviours measured at 4-6-years. Concurrently measured depressive symptoms when children were 4-6-years was negatively associated with RCPM scores. K-means cluster analysis revealed that persistently high maternal depressive symptoms since pregnancy posed the highest risk for children's low RCPM scores and high SDQ internalizing scores.
Of note, maternal depression showed no significant associations with externalizing symptoms.

Conclusions:
Maternal depressive symptoms, particularly during the postnatal period, have profound and lasting effects on children's cognitive and mental health outcomes, with persistently high symptoms associated with the worst outcomes during middle-childhood. Our longitudinal study highlights the urgent need to extend maternal mental health interventions beyond the perinatal period to mitigate long-term developmental risks.

Funding:
DBT/Wellcome Trust India Alliance Team Science Grant [Grant No. IA/TSG/20/1/600023]

Key-words: (up to 5):
maternal depression, child development, middle-childhood, cognitive outcomes, internalizing behaviours

Abstract #00006703 en

Bioinformatic characterization and identification of transposable elements in the trophoblast

Structure and Function of the Placenta as a Regulator of Health in the Next Generation

Campos-Arellano David Eduardo (1), Flores-Torres Mariana (2), Cristóbal Fresno (3), Chavira-Suárez Erika (4)
(1) National Autonomous University of Mexico, (2) National Institute of Genomic Medicine, (3) Anahuac University of Mexico, (4) National Autonomous University of Mexico / Anahuac University of Mexico

Background/aims:
Interactions between transposable elements (TEs) and other molecules may be a regulatory mechanism of placental function. Currently, there are no standardized bioinformatic strategies for evaluating placental TEs in a massive data format. This study aims to utilize innovative bioinformatic methods to characterize the profiles of trophoblast TEs.

Methods:
Whole genome sequencing (WGS) of first trimester trophoblast cells (n=10) was used to identify and characterize TEs in the trophoblast genome using available data sets from the Sequence Read Archive, European Nucleotide Archive, and Genome Sequence Archive databases. The hg38 human genome sequence served as a reference, and WGS data sets of cancer cells from the liver, colon, and breast were also examined as groups with altered TEs conformation. The xTea v0.1.6 program was employed to identify the TEs families that were not noted in hg38. Subsequently, the abundance was normalized to reads per million (RPM). Utilizing Rv4.3.0, the xTea data was manipulated and visualized.

Results:
The trophoblast and cancer genomes and chromosomes contain the Alu, L1, and SVA families in varying quantities and proportions. The abundance of trophoblast TEs (~5 RPM) is less than that of cancer cells in the breast (~10 RPM), colon (~23 RPM), and liver (~35 RPM). In the trophoblast, the intergenic and intron regions of the genome contain 90% of the Alu, L1, and SVA family proportions. Nevertheless, the proportion of Alu insertions in exon regions is higher in trophoblast cells (4%) than in cancer cells (1-2%), whereas Li insertions in exon regions are exclusively present in liver and colon cancer cells.

Conclusions:
A bioinformatic pipeline was developed to investigate the mechanisms of placental function and their impact on developmental programming by examining TEs in the trophoblast genome.

Funding:
CONAHCYT 319605 awarded to EC-S

Key-words: (up to 5):
Developmental programming, DOHaD concept, whole genome sequencing, placental function

Abstract #00006706 en

The One Health Significance of Antimicrobial Resistance in Enterobacterales from Female Companion Animals

Plant and Animal Health and Its Impact on Reproductive Age Individuals and Their Offspring

DARINI ANA LUCIA (1), Cabral Stella (2), Ramos Carolina Aparecida (2), Ferreira Joseane Cristina (2), Barth Patricia Orlandi (3), Barth Afonso Luís (3), Ballaben Anelise Stella (4)
(1) UNIVERSITY OF SÃO PAULO, (2) School of Pharmaceutical Sciences of Ribeirao Preto, University of Sao Paulo, (3) Bacterial Resistance Research Laboratory, Clinics Hospital of Porto Alegre, (4) Faculty of Agricultural and Veterinary Sciences-Jaboticabal, Sao Paulo State University

Background/aims:
Health threats, such as antimicrobial resistance, can directly impact females animals of reproductive age, potentially affect their offspring or future generations. Additionally, the close contact between pets and their guardians may facilitate the transmission of antimicrobial-resistant bacteria, highlighting the relevance of this issue from One Health perspective.

Methods:
To investigate the presence of antibiotic-resistant Enterobacterales, rectal swabs were collected from 32 clinically healthy female dogs and 39 cats living in households in Ribeirão Preto-SP, Brazil. None of these animals had received antibiotic treatment within the 30 days prior to sampling. Bacterial isolates were selected using MacConkey agar (+2 µg/mL cefotaxime). Identification was performed by MALDI-TOF MS and Klebsiella MALDI TypeR platform and antimicrobial susceptibility was accessed by disk diffusion with 14 antibiotics. ESBL production was detected using double-disk synergy test, and PCR was employed to detect 42 resistance genes (beta-lactamases, quinolones, fluoroquinolones, aminoglycosides and polymyxins).

Results:
A total of 27 Enterobacterales were isolated from 21 dogs, and 9 from 7 cats. Escherichia coli and Klebsiella pneumoniae complex were the most frequently identified bacteria. Hafnia alvei was isolated from a female cat, while Enterobacter spp. (n=4), Citrobacter freundii (n=2), and Proteus mirabilis (n=1) were isolated from female dogs. Multidrug resistance (MDR) was more prevalent among canine isolates (59%) than among feline isolates (67%). Tetracycline resistance was observed more frequently in canine isolates, while sulfamethoxazole/trimethoprim resistance predominated among feline ones. No isolate showed resistance to polymyxin. blaCTX-M-1 was the most prevalent gene among the isolates of both species; blaSHV, blaTEM and aac(6')-Ib genes were also detected.

Conclusions:
From a One Health perspective, the detection of antimicrobial-resistant Enterobacterales in healthy companion animals reinforce their role as reservoirs and disseminators of resistance genes. These findings emphasize the importance of integrated surveillance strategies to preserve ecosystem balance and safeguard both animal and human health.

Funding:
FAPESP 2024/16604-7; INCT – MCTI/CNPq/CAPES/FAPs nº 16/2014. S.C -M.Sc fellowship - FAPESP 2024/01213-2, C.A.R - doctoral fellowship CAPES 88887.115345/2025-00, and A.S.B -post-doctoral fellowship FAPESP 2023/08702-6.

Key-words: (up to 5):
One Health, antimicrobial resistance, Enterobacterales, female cats, female dogs

Abstract #00006707 en

Joint contribution of air pollution and neighborhood deprivation to trajectories of adolescent mental health in the ABCD Study

Big Data and Cohorts in DOHaD Research.

Chaney Carlye (1), Wiley Kyle (2)
(1) University of Missouri and Washington University in St. Louis, (2) University of Texas, El Paso

Background/aims:
Adolescence – a developmental stage with a high risk for the emergence of mental health problems – is a sensitive period in which brain development is susceptible to environmental exposures. Previous research demonstrates that mental health is influenced by air pollution and neighborhood deprivation. However, most of this work uses cross-sectional assessments of mental health and is not focused on adolescence. In this study, we quantified the contributions of air pollution and neighborhood deprivation to trajectories of adolescent mental health in the Adolescent Brain and Cognitive Development (ABCD) study, focusing on internalizing behaviors.

Methods:
We analyzed data from children aged 9 to 13 across four annual waves of the ABCD Study (n = 6,585), including longitudinal data on Child Behavior Checklist scores as well as each child's predicted exposure to particulate matter (PM) with a diameter of 2.5 microns or less based on their address. We created latent class linear mixed models in the 'lcmm' package in R and investigated which variables best predicted class membership and trajectory using multinomial logistic regression in 'nnet'.

Results:
Seven classes fit the data best based on AIC and BIC. For PM2.5 exposure, the interaction between PM2.5 and neighborhood deprivation was associated with being in a higher internalizing score class (OR range 2.58-8.51, p-value range <0.001-0.009, depending on class). PM2.5 and area deprivation also had significant independent effects on internalizing behavior.

Conclusions:
PM2.5 exposure and neighborhood deprivation at ages 9-10 is associated with greater internalizing behaviors across adolescence. Further, the interaction between PM2.5 and neighborhood deprivation was associated with greater odds ratios of belonging to a higher internalizing score class than either variable alone. These findings suggest that air pollution and neighborhood deprivation may have synergistic effects on internalizing disorders, such as anxiety and depression, in adolescence.

Funding:
Funding: NSF SPRF #2313258

Key-words: (up to 5):
air pollution; neighborhood deprivation; adolescence; internalizing symptoms

Abstract #00006708 en

Striatal SLC6A3 co-expression gene network moderates the effect of low birth weight on inflammation in young children, defining risk for metabolic and psychiatric comorbidities later in lif

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Rosenblatt Andrew M. (1), Pokhvisneva Irina (2), Elgbeili Guillaume (2), Slopen Natalie (3), Williams David R. (4), Bush Nicole R. (5), Levitt Pat (6), Gunnar Megan R. (7), Meaney Michael J. (2), Shonkoff Jack P. (3), Silveira Patrícia Pelufo
(2)
(1) UCSF School of Medicine, University of California, San Francisco, (2) Douglas Mental Health University Institute, McGill University, (3) Harvard T.H. Chan School of Public Health, Harvard University, (4) Harvard T.H. Chan School of Public Health, Harvard University, (5) UCSF Weill Institute for Neurosciences, (6) Keck School of Medicine, University of Southern California, (7) Institute of Child Development, University of Minnesota

Background/aims:
Early life adversity influences the risk of developing metabolic and psychiatric comorbidities later in life. However, not every child exposed to adversity will develop disease. We recently described that a gene network centered on the dopamine transporter gene (SLC6A3), quantified through an expression-based polygenic score (ePRS), moderates the effect of low birth weight on the risk for metabolic and psychiatric comorbidities in adolescents and adults. Specifically, individuals born with lower birth weight exhibited elevated risk within the low ePRS group (Barth et al., 2024).

Methods:
We investigated if the SLC6A3 network is associated with biomarkers of risk in early childhood. Children from the Healthy Early Roots and Origins (HERO study) were evaluated for the identification of biomarkers of stress activation between birth and 5 years of age (N=728) using polygenic risk scores.

Results:
We observed that the SLC6A3 ePRS moderated the effect of low birth weight on the pro-inflammatory cytokine interleukin-8 (IL-8) (SLC6A3 ePRS*low birth weight interaction, b=-0.38, P=0.02), in which the high ePRS group had lower and the low ePRS group (with risk for disease in adolescence and adulthood) had higher IL-8 levels, but not other cytokines (IL-6, IL1B).

Conclusions:
IL-8 has been linked to poor neonatal outcomes in low birth weight children. This work underscores that IL-8 may also mediate the effect of low birth weight on later health outcomes in individuals with lower expression of the striatal SLC6A3 gene network. Dopaminergic regulation is a critical mechanism through which early adversity influences lifelong health, and salivary IL-8 as an important biomarker of these associations.

Funding:
JPB Foundation and FRQS **Key-words: (up**

to 5):

Early-life adversity, Dopamine transporter (SLC6A3), Polygenic risk score, Interleukin-8 (IL-8), Low birth weight

Abstract #00006709 en

Low-Dose Parental NDMA Exposure Impacts Male F1 Parameters in Wistar Rats

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Stein Julia (1), Nagaoka Lívia Trippe (1), Castro Reggina Lorena Mellado (1), Rosalem Giovanna Ferrari (1), Aquino Júlia Vitória Francisco (1), Alves Júlia Tavares (1), Vitale Otávio Galassi (1), Marraschi Giovanna Kugel (1), Santos Sara Tawany Caetano (1), Magalhães Luara (1), Jorge Bárbara Campos (1), Arena Arielle Cristina (1) (1) Institute of Biosciences of Botucatu (IBB) - São Paulo State University (UNESP)

Background/aims:
Parental exposure to xenobiotics can impact future generations, forming the basis of the DOHaD and POHaD hypothesis. Nitrosodimethylamine (NDMA) is a widespread environmental pollutant to which people are unknowingly exposed through various life's stages. While high doses are carcinogenic and mutagenic, their long-lasting impacts in acceptable daily intake exposures remain unclear. We aimed to evaluate the toxicological and reproductive effects of parental NDMA exposure on male F1 rats.

Methods:
F0 male and females Wistar rats received either control (distilled water, 1mL/kg/day) or NDMA (7.2 ng/kg/day) from postnatal day (PND) 60 until mating. Females continued exposure through gestation and lactation. Four groups were formed: C (control males X control females); M (NDMA females X control males); P (control females X NDMA males); and MP (NDMA females X NDMA males). Male F1 offspring were evaluated in sexual development, and reproductive and toxicological parameters at PND 70, always compared to C group (ethics Committee: 470426042).

Results:
In early sexual development, body weight at PND 1 in the P group increased but was normalized at PNDs 13 and 22. The day of testicular decent in the MP group was delayed. At PND 22, there were no changes in organ weight and hematological analyses. At PND 70, the absolute and relative weight of the full seminal gland increased in the P group. In histological evaluations the staging of the seminiferous tubules did not show any changes but there was an increase in the area, volume and number of nuclei of Leydig cells in the P group, and an increase in the number of these cells in the MP group.

Conclusions:
Environmentally relevant NDMA exposure, especially via paternal line, induced changes in male F1 rats, supporting POHaD hypothesis.

Funding:
FAPESP (2022/15849-0; 2022/15364-7); CAPES (88887.809658/2023-00)

Key-words: (up to 5):
Nitrosamines, POHaD, Toxicology, Leydig cells

Abstract #00006711 en

Characterization of hematological and iron biomarkers in anemic children aged 6–59 months: Brazilian National Survey on Child Nutrition (ENANI-2019)

Public Health Policies Across the Life Cycle.

Vicente Lucas Goldenberg (1), Normando Paula (1), Freitas-Costa Nathalia Cristina (1), dos Santos Isabel Nascimento (1), Peixoto Karine de Souza (1), Machado Raquel Schincaglia (2), Castro Inês Rugani Ribeiro de (3), Freire Samary da Silva Rosa (1), Rodrigues Driele (1), Kac Gilberto (1)
(1) Institute of Nutrition Josué de Castro, Federal University of Rio de Janeiro, (2) Faculty of Nutrition, Federal University of Goias, (3) Institute of Nutrition, State University of Rio de Janeiro

Background/aims:
Anemia remains a significant public health concern among children under 5 years of age worldwide. It is therefore essential to identify its etiology. This study evaluated hematological and iron biomarkers in Brazilian children.

Methods:
A subset of 979 children aged 6–59 months from the ENANI-2019 was analyzed. Biomarkers of iron were evaluated: Hemoglobin, Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Soluble Transferrin Receptor (sTfR), Ferritin, and Hepcidin. The sTfR/log Ferritin ratio was calculated. Iron deficiency anemia (IDA) and non-iron deficiency anemia (NIDA) were defined according to WHO criteria. Differences in biomarker median concentrations among IDA, NIDA, and non-anemic (non-A) groups were evaluated using the Kruskal-Wallis test, followed by Dunn's post hoc test with Bonferroni correction. P-values <0.05 were considered statistically significant. Ethics-approved; informed consent obtained for all participants (CAAE:89798718.7.0000.5257).

Results:
Hemoglobin concentrations were significantly lower in the IDA and NIDA groups (9.8, 10.2 g/dL) compared to non-A (12.1 g/dL, P<0.001). MCV and MCH were significantly lower in the IDA group (66.3 μm^3; 21.2 pg) compared to the NIDA (73.4 μm^3; 24.1 pg) and non-A groups (77.1 μm^3; 25.9 pg; P<0.001). sTfR was significantly higher in the IDA group compared to NIDA and non-A (3.5, 2.0 and 2.0 mg/L; P<0.001). Ferritin was significantly lower in the IDA group than in NIDA and non-A (5.7, 19.2 and 22.2 ng/mL; P<0.001). Hepcidin were also significantly lower in IDA compared to NIDA and non-A (2131.0, 11613.0 and 13198.0 pg/mL; P<0.001). The sTfR/log ferritin ratio was significantly higher in the IDA group than in NIDA and non-A (2.2, 0.7 and 0.6; P<0.001).

Conclusions:
The IDA group was characterized by lower MCV, MCH, ferritin, and hepcidin, and higher sTfR concentrations. Our results suggest that NIDA may be due to anemia of inflammation, given the elevated ferritin and hepcidin concentrations, and the low sTfR/log ferritin ratio in this group.

Funding:
Brazilian Ministry of Health/ Brazilian National Research Council (CNPq).

Key-words: (up to 5):
anemia; iron metabolism; national survey

Abstract #00006718 en

The demographic transition in Chile

Public Health Policies Across the Life Cycle.

Mardones Francisco (1), Caulier Cisterna Raul (2), Donoso Manuel (3)
(1) School of public Health, Pontificia Universidad Católica de Chile, (2) Universidad Tecnológica Metropolitana, (3) Department of Obstetrics, Gynecology and Reproductive Biology, Universidad de los Andes, Chile.

Background/aims:
The demographic transition consists of the substitution of slow population growth, achieved with high fertility and mortality rates, for sustained slow growth with relatively low fertility and mortality rates. A universal demographic transition toward population aging is evident. In Latin America infant mortality started to decline in the first half of the twentieth century, while birth rates remained high but declined in the second half of the 20th century. The demographic transition in Chile is presented.

Methods:
We reviewed official information and the scientific literature.

Results:
At the beginning of the 20th century, the infant mortality rate (IMR) was very high and did not improve; between 1924 and 1936 it remained stable hovering around 220. It declined in close association with the expansion of public primary health care between 1937 and 1950 (r value: 0.9). Its coverage continued to be expanded and increased from 80% in 1986 to nowadays 99.9% of the population. IMR in year 2024 is 6.2. Family planning policy began in 1966 aiming to reduce the high maternal mortality figure. Fertility has declined considerably: the fecundity rate was 5.4 children per woman in 1960-65 while in 1990-1995 reached a figure of 2.1. Moreover, in 2024 it has fallen to 1.03 children per woman, representing one of the lowest rates in the world. The last public policy that has attempted to increase fertility was begun in 2011: it increased maternity leave from 12 to 24 weeks postpartum. It has been associated with an increase in the duration of breastfeeding but has not been associated with an increase in fertility.

Conclusions:
Chile is currently undergoing a demographic transition with a growing population over 65. The current challenges are how to improve the fertility rate to avoid the problems faced by societies with a growing population requiring more healthcare.

Funding:
None.

Key-words: (up to 5):
Demographic Transition, Infant Mortality, Maternal Mortality, Fertility, Aging, Chilean people.

Abstract #00006722 en

Modulatory Effects of Allium cepa Linn. Juice and Mechanisms of Action Against Alterations in Uterine Functions in Ibuprofen-exposed Wistar Rats.

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Adegbite Latif Opeyemi (1), Raji Yinusa (2) (1) Osun State University, (2) University of Ibadan

Background/aims:
Although linked to reproductive problems, ibuprofen is extensively used as an analgesic. Consuming Allium cepa L. improves reproductive functioning through oestrogen. However, its effects on uterine functioning are unclear. This study examined how Allium cepa L. juice modulates uterine functions in ibuprofen-exposed rats.

Methods:
Forty rats grouped (n=10) and treated orally as follows: Groups I-control; distilled water(10mL/kg), II-ibuprofen(500mg/kg), III-Allium cepa L. juice; ACJ(500mg/kg), IV-ibuprofen+ACJ. Oestrous cycle was monitored using Marcondes' technique. After 28 days of administration, rats were sacrificed at oestrus phase. Serum levels of reproductive hormones, markers of oxidative stress and inflammation were measured using standard methods. Uterine Ki-67, oxytocin receptor and α-Smooth Muscle Actin (α-SMA) expressions were assessed using immunohistochemistry. Endometrial thickness, glandular density, and collagen fibre were assessed using microscopy. Uterine steroid Receptors expressions were assessed using Western blotting. Ex-vivo, uterine smooth muscle contractions were evaluated using data acquisition capsule.

Results:
Irregular oestrous cycle in II was ameliorated in IV. Serum FSH (0.33±0.02vs0.24±0.01mIU/mL),LH(0.27±0.02vs0.12±0.01mIU/mL),oestradiol(18.55±0.97vs13.42±0.65p g/mL) and progesterone(75.25±11.77vs34.00±3.17ng/mL) significantly increased in IV compared with II. Serum TNF-α(3.36±0.28vs4.337±0.32pg/mL) significantly decreased in IV compared with II. Malondialdehyde significantly decreased(5.27±0.17vs8.15±0.72mU/mL) while SOD(0.73±0.01vs0.31±0.01U/mL), catalase(21.20±1.72vs6.58±0.62U/mL) and
GPx(11.54±0.31vs2.28±0.34U/mL) significantly increased in IV relative to II. Uterine oxytocin receptor and α-SMA were down-regulated in III and IV compared with control. Glandular density significantly reduced in II compared with control (7.00±0.89vs11.00±0.45glands/μm2) and significantly increased in IV relative to II (15.40±1.47vs7.00±0.89glands/μm2). Collagen fibre was up-regulated in II relative to control and down-regulated in IV compared with II. Uterine ER-α and PR expressions were down-regulated in II relative to control and up-regulated in IV compared with II. The ACJ significantly inhibits oxytocin-induced uterine contraction by reducing the amplitude (1.13±0.24vs4.86±0.35g) and frequency (0.01±0.00vs0.02±0.00Hz) of contraction compared with control.

Conclusions:
Allium cepa L. juice increased antioxidant, anti-inflammatory and endocrine activities, improved uterine histoarchitecture, and enhanced tocolysis in ibuprofen-exposed rats.

Funding:

TETFUND Nigeria

Key-words: (up to 5):
Ibuprofen, Allium cepa L., steroid receptors, uterine functions, tocolysis.

Abstract #00006725 en

Fish oil during gestation and lactation protects offspring from visceral obesity and BAT lipid accumulation caused by maternal high-fat diet

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Neto Jessika Geisebel (1), Woyames Juliana (1), Tatagiba Maria Catarina (1), Sousa Rafaela (1), Fassarella Larissa (1), Trevenzoli Isis (1), Pazos-Moura Carmen (1)
(1) Universidade Federal do Rio de Janeiro

Background/aims:
Perinatal maternal high-fat diet (mHF) is associated with increased susceptibility to obesity. Fish oil (FO, n-3 PUFA source) reduces serum lipids and adiposity, and adolescent mHF offspring treated with FO had long-term metabolic benefits. This study aimed to evaluate the potential benefits of FO given to rats during gestation and lactation on adiposity and lipid accumulation of the offspring at weaning and its programming effects during adolescence.

Methods:
Female Wistar rats received control (CT: 9% from fat) or high-fat diet (HF: 39% from fat) prior to mating and throughout pregnancy and lactation. A subset of HF-fed dams received FO supplementation (HFFO:
3% of FO added to the diet) during pregnancy and lactation (Ethic committee #135/22).

Results:
At weaning (21d), the maternal HF led to increased visceral (P<0,0001 vs CT♂; P<0,0001 vs CT♀) and subcutaneous (P<0,0001 vs CT♂; P<0,0001 vs CT♀) adiposity in offspring. Additionally, HF increased brown adipose tissue (BAT) mass (P=0,001 vs CT♂) and lipid content (P=0,002 vs CT♂), accompanied by elevated interscapular temperature (P=0,038 vs CT♂) in males only. FO supplementation reduces circulating triacylglycerol levels in both sexes (P=0,043 vs HF♂; P=0,026 vs HF♀). FO attenuates adiposity, BAT mass and reduces BAT lipids (P<0,0001 vs HF♂) in males. FO also increased interscapular temperature in males (P=0,014 vs CT♂) and leads to a tendency for increasing in females (P=0,068 vs CT♀). At adolescence (45d), maternal HF programs for increased visceral adiposity in males (P=0,039 vs CT♂) and FO was able to attenuate this phenotype. Maternal FO supplementation programs for reduced BAT lipid content (P=0,015 vs HD♀) and leads to a tendency for reduced BAT mass (P=0,067 vs HD♀) only in females.

Conclusions:
Maternal FO supplementation exerts sex-specific protective effects on the offspring, supporting n-3 PUFA intervention to reprogram metabolism and protect from long-term adverse outcomes induced by maternal HF diet.

Funding:
Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ) , Brazil and by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Brazil

Key-words: (up to 5):
Key-words: Metabolic programming, Maternal obesity, Lipid metabolism, Thermogenesis.

Abstract #00006726 en

Multigenerational NDMA Exposure: Developmental, Toxicological, and Reproductive Outcomes in F2 Wistar Rats Indirectly Exposed via F1 Maternal Lineage

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Nagaoka Lívia Trippe (1), Stein Julia (1), Vitale Otávio Galassi (1), Marraschi Giovanna Kugel (1), Aquino Júlia Vitória Francisco de (1), Castro Reggina Lorena Mellado (1), Rosalem Giovanna Ferrari (1), Santos Sara Tawany Caetano dos (1), Magalhães Luara (1), Alves Júlia Tavares (1), Jorge Bárbara Campos (1), Arena Arielle Cristina (1) (1) Institute of Biosciences of Botucatu (IBB), São Paulo State University (UNESP)

Background/aims:
Nitrosodimethylamine (NDMA) is a byproduct of industrial production and a widespread environmental contaminant found in various sources, including drinking water and polluted air. Although high-dose NDMA exposure has been associated with carcinogenicity and mutagenicity, the multigenerational effects of exposure to low doses remain unclear. This study aims to evaluate the multigenerational effects of indirect exposure to NDMA on developmental and toxicological parameters in rats.

Methods:
Male and female F0 Wistar rats were daily exposed to water (1 mL/kg) or NDMA (7.2 ng/kg) from preconception to lactation. F1 female offspring was mated with unexposed males to produce the F2 generation, which was evaluated for initial development and pubertal onset parameters, and later euthanized for organ and blood collection (Ethics Committee: 4704260423).

Results:
F2 Males from the NDMA group had increased body weight on postnatal days (PND) 1, 13, and 22, decreased relative anogenital distance (AGD) on PND 1, and increased absolute AGD on PND 22. F2 females had increased body weight on PND 13 and 22. On puberty onset parameters, NDMA males had delayed testicular descent and were heavier at descent. Females showed prolonged metestrus, in the estrous cycle analysis. At PND 70, males had increased absolute spleen and thyroid weights, decreased relative testis weight, increased body weight, and reduced hematocrit. At PND 110, males showed reduced absolute weight of empty seminal vesicles and reduced relative weights of both empty and full vesicles. At PND 100, females had reduced absolute ovary and spleen weights, but showed no hematological changes.

Conclusions:
These findings suggest that multigenerational low-dose NDMA exposure is capable of altering growth, sexual maturation, and organ development in a sex- and age-dependent manner.

Funding:
FAPESP (2022/15364-7; 2024/04466-9); CAPES(88887.806581/2023-00).

Key-words: (up to 5):
NDMA, multigenerational, toxicology, DOHaD.

Abstract #00006727 en

Rapid weight gain and its influence on obesity in childhood: findings from the 100 million Brazilian Cohort

Big Data and Cohorts in DOHaD Research.

Batista Tonaco Luis Antonio (1), Narumi Klara (2), Santiago-Vieira Carolina (3), Pinto Elizabete de Jesus (4), Ribeiro Silva Rita de Cássia (5), Dias Moreira Alexandra (2), Aguiar Sofia (2), Felisbino-Mendes Mariana (2), Velasquez-Melendez Gustavo (2)
(1) Universidade Federal de MInas Gerais, (2) Universidade Federal de Minas Gerais, (3) CIDACS, (4) Universidade Federal do Reconcavo da Bahia , (5) Universidade Federal da Bahia

Background/aims:
From the global estimates indicate that more than 37 million children under five years old were overweight or obese globally. Reducing the prevalence of overweight is a key target in the global plan to reduce obesity. .Objective: To examine the role of rapid weight gain (RWG) in risk of obesity by age 9, using administrative data from the 100 million Brazilians Cohort.

Methods:
A population-based cohort from the Cadastro Único (CadÚnico) based on the linkage of the National Live Births System (SINASC) and the National Food and Nutritional Surveillance System (SISVAN). The sample comprised 33.657 Brazilian children aged from zero to 9 years . We derived the difference between the last weight-for-age (WAZ) z-scores measurement before the age of 2 and the WAZ at birth to calculate the rapid weight gain (RWG). Obesity was defined using WHO criteria (z-WAZ>2) . Logistic regression were used to estimate the odds of obesity at 9 years and 95% Confidence Intervals, comparing six categories of
RWG.

Results:
A total of 6.1% of children experienced RWG before 2 years old. The prevalence of obesity was 11.9%. Compared to children with stable weight gain (reference group), increasing categories of early weight gain were strongly associated with higher odds of later obesity. Adjusted odds ratios (95% CI) were 1.02 (0.88–1.21), 1.21 (1.05–1.40), 1.46 (1.27–1.69), 1.90 (1.65–2.19), and 2.75 (2.40–3.16), indicating a clear dose–response relationship.

Conclusions:
A gradient in the z-score of weight gain from birth to 2 years of age was associated with higher odds of overweight and obesity. These findings highlight the importance of monitoring early growth trajectories as predictors of future obesity. The present study supports that RWG during infancy is a significant predictor of adiposity indices by age 9; however, further research is needed to explore the association between early rapid growth and obesity later in adulthood.

Funding:
CNPq /CGFP/DECIT/ SECTICS (Processo 406513/2024-4) e FAPEMIG (APQ-01777-23 and FAPEMIG/DCTI nº. 40068203/2021

Key-words: (up to 5):
Obesity, child, rapid weight growth

Abstract #00006728 en

Maternal and newborn dyads: transfer of anti-SARS-CoV-2 antibody in a cross sectional study

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Trujillo Janet (1), Correa Matías (2), Madamo Agustina (2), Colomar Mercedes (2), Barrios Anabella (3), Pirez Macarena (3), Alvarez Cecilia Beatriz (2), Gonzalez-Sapienza Gualberto (3), Alemán Alicia (2)
(1) Unidad académica de Medicina Preventiva y Social, Facultad de Medicina, Universidad de la República., (2) Unidad académica de Medicina Preventiva y Social, Facultad de Medicina, Universidad de la República, (3) Cátedra de Inmunología, Facultad de Química, Instituto de Higiene, Universidad de la República.

Background/aims:
In pandemic context, pregnant women acquired immunity through COVID-19 infection or vaccines, but newborn immunity depended on the placental transfer of antibodies. The aim was to establish the relationship between maternal and newborn anti-SARS-CoV-2 antibody levels in those deliveries attended in the Pereira Rossell Hospital, in Uruguay.

Methods:
It is a cross-sectional study of pregnant women, and their newborn enrolled from the Pereira Rossell Hospital, Montevideo, Uruguay, between February and March of 2023. The inclusion criteria were pregnant women admitted to the hospital to deliver with a pre-labor blood sample, and their newborn born alive with an umbilical cord sample. Women with immunocompromised diseases and multiple births were excluded. The anti-SARS-CoV-2 antibody levels were measured by ELISA. The study was approved by the Pereira Rossell Hospital Ethical Committee and all mothers gave their informed consent. Descriptive and correlation analysis were developed.

Results:
A total of 148 mother-newborn dyads were studied. There were 54 (36,5%) pregnant women who reported having had COVID-19, and from these, 12 in pregnancy. Only 127 pregnant women received COVID-19 vaccines. The median of anti-SARS-CoV-2 antibodies levels were 1873,5 (IQR=2772,7) and 2511,2 (IQR= 3117,0) BAU/ml for mother and newborn, respectively. The maternal to fetal transfer median ratio was 1,33 (IQR=0,94), no statistical differences were found between newborn sex (p=0,1165) and for those born from mothers having had COVID-19 in pregnancy or before (p=0,671) or vaccinated (p=0,741). Also, there were no differences in levels of anti-SARS-CoV-2 antibodies for those groups. The Kendall-Tau correlation between maternal and newborn antibodies against SARS-CoV-2 was 0,632 (p<0,0001).

Conclusions:
These findings support the immunity protection given by mothers to babies through maternal COVID-19 infection and vaccination and the feasibility to do surveillance with discarded human blood.

Funding:
The study was supported by the Pan American Health Organization (PAHO/WHO, 2022) and the Latin American Center of Perinatology (CLAP, 2022).

Key-words: (up to 5):
virus SARS-CoV-2, antibody, newborn, pregnant woman, vaccine.

Abstract #00006729 en

Nitrosodimethylamine (NDMA): Developmental and Toxicological Effects in F2 Wistar Rats Indirectly Exposed via Paternal F1 Lineage

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Nagaoka Lívia Trippe (1), Stein Julia (1), Vitale Otávio Galassi (1), Marraschi Giovanna Kugel (1), Aquino Júlia Vitória Francisco de (1), Castro Reggina Lorena Mellado (1), Rosalem Giovanna Ferrari (1), Santos Sara Tawany Caetano dos (1), Magalhães Luara (1), Alves Júlia Tavares (1), Jorge Bárbara Campos (1), Arena Arielle Cristina (1) (1) Institute of Biosciences of Botucatu (IBB), São Paulo State University (UNESP)

Background/aims:
Nitrosodimethylamine (NDMA), a nitrosamine resultant of industrial production processes, is a common environmental pollutant present in sources such as drinking water, processed food and polluted air. While its carcinogenic potential at high doses is well established, the impacts of multigenerational low-dose exposure are not fully understood. This study investigates the multigenerational effects of indirect paternal NDMA exposure on developmental and toxicological outcomes in rats.

Methods:
In this study, F2 generation was exposed indirectly to NDMA via the germline cells of F1 males, directly exposed through the F0 males and females, which received daily oral doses of either water (1 mL/kg) or NDMA (7.2 ng/kg) from the preconception period up until lactation. F1 males were then mated with unexposed females to obtain the F2 generation. F2 animals were assessed for early development and pubertal onset, followed by euthanasia for organ and blood collection (Ethics Committee: 4704260423).

Results:
At postnatal day (PND) 1, NDMA group F2 females showed reduced body weight. No significant changes were observed in puberty onset parameters in either sex. At PND 60, females had increased absolute ovarian weight, and on PND 70 F2 males exhibited increased mean corpuscular volume. In adult males, on PND 110, NDMA indirect exposure led to reduced absolute and relative thyroid weights, as well as decreased relative weights of the testis, epididymis, prostate, and duct deferens. Additionally, hematocrit levels were elevated. In females, at PND 100, uterine and kidney absolute weights were increased, along with final body weight.

Conclusions:
These findings indicate that indirect low-dose NDMA exposure through the paternal lineage may alter hematological and organ weight parameters in a sex-specific and age-dependent manner, even in the absence of signs of delayed puberty.

Funding:
FAPESP (2022/15364-7; 2024/04466-9); CAPES(88887.806581/2023-00)

Key-words: (up to 5):
NDMA, multigenerational, POHaD, DOHaD.

Abstract #00006730 en

Questioning the Safety Threshold: Effects of Acceptable NDMA Exposure in female offspring in Wistar rats

Impact of Early Life Exposures and Environmental Pollutants

Stein Julia (1), Nagaoka Lívia Trippe (1), Rosalem Giovanna Ferrari (1), Castro Reggina Lorena Mellado (1), Aquino Júlia Vitória Francisco (1), Alves Júlia Tavares (1), Vitale Otávio Galassi (1), Marraschi Giovanna Kugel (1), Santos Sara Tawany Caetano (1), Magalhães Luara (1), Jorge Bárbara Campos (1), Arena Arielle Cristina (1) (1) Institute of Biosciences of Botucatu (IBB) - São Paulo State University (UNESP)

Background/aims:
Infertility is deeply correlated to environmental and lifestyle factors. The DOHaD and POHaD hypotheses emphasize the influence of parental health on offspring. Nitrosodimethylamine (NDMA), a widespread environmental contaminant in water, food, and pharmaceuticals, has mutagenic, genotoxic, and carcinogenic properties, besides being able to generate reactive oxygen species. However, data on its reproductive and developmental toxicity, particularly at low doses remain limited. Our aim was to investigate the impact of prolonged NDMA exposure on toxicological and reproductive outcomes in female F1 rats.

Methods:
Wistar rats received distilled water (control - 1mL/kg/day) or NDMA (7.2 ng/kg/day). F0 generation was assigned to four groups: C (control males X control females); M (NDMA females X control males); P (control females X NDMA males); and MP (NDMA females X NDMA males), exposed from postnatal day (PND) 60 until mating. Females remained exposed throughout gestation and lactation. Female F1 offspring were exposed from PND 22 to 60, with 1 pup/sex/litter exposed to control (groups -) and the other to NDMA (groups +). Adult F1 females were assessed for reproductive and toxicological parameters (ethics Committee: 470426042).

Results:
Estrous cycle, sexual behavior, organ weight, hematology and follicle count were unaffected. However, alkaline phosphatase decreased in the P- and P+ groups and gamma glutamyl transferase increased in the M+ group. In the fertility test, MP- group reduced uterus + fetuses' weight, the number of implantations and live fetuses. Superoxide dismutase (SOD) activity was reduced in the M-, P-, MP-, C+ and M+ groups, while catalase (CAT) and glutathione (GSH) decreased in P+ group.

Conclusions:
Even at low doses, NDMA exposure led to changes in female offspring, emphasizing the importance of parental environmental health and the need to re-evaluate current safety limits.

Funding:
FAPESP (2022/15849-0; 2022/15364-7); CAPES (88887.809658/2023-00)

Key-words: (up to 5):
Nitrosodimethylamine, Oxidative stress, fertility

Abstract #00006731 en

Association of heavy metals with TSH and thyroid hormones in maternal and cord blood: findings from a cohort (PIPA Study)

Big Data and Cohorts in DOHaD Research.

Andrade Marcelle Novaes (1), Bertasso Iala Milene (2), Souza Clara Martins Rollemberg (3), Figueiredo Nataly Damasceno (4), Asmus Carmen Ildes Rodrigues Fróes (4), Moura Egberto Gaspar (2), Carvalho Denise Pires (5), Lisboa Patrícia Cristina (2), Miranda-Alves Leandro (1)
(1) Instituto de Ciências Biomédicas - Universidade Federal do Rio de Janeiro, (2) Instituto de Biologia - Universidade do Estado do Rio de Janeiro, (3) Instituto de Estudos em Saúde Coletiva - Universidade Federal do Rio de Janeiro, (4) Maternidade Escola, Faculdade de Medicina - Universidade Federal do Rio de Janeiro, (5) Instituto de Biofísica Universidade Federal do Rio de Janeiro

Background/aims:
Heavy metals, such as lead, mercury, cadmium and arsenic, are considered endocrine-disrupting chemicals of global concern due to their toxic effects on human health and the environment, including affecting the thyroid gland and potentially causing thyroid disorders. The aim of the study was to evaluate the relationship between in utero exposure to the heavy metals (lead, mercury, cadmium and arsenic) with thyrotropin (TSH) and thyroid hormones (TH) at birth.

Methods:
The study population consisted of 99 mother-infant pairs from the birth cohort of the Childhood and Environmental Pollutants Project (PIPA-UFRJ) from Rio de Janeiro, recruited between June 2021 and July 2022. Metals were analyzed using inductively coupled plasma mass spectrometry (ICP-MS) in umbilical cord blood. Hormones in maternal plasma and cord blood were measured using ELISA or Multiplex Assay. Spearman's correlation was used to evaluate the relationship between metal and hormone. Linear regression analysis was performed to assess the association between metal exposure, hormone levels, and weight gain (CEP: 5.415.164).

Results:
The detection rates of metals in umbilical cord blood samples were lead (100%), mercury (93.8%), arsenic (59.2%), and cadmium (13.3%). Arsenic concentration in umbilical cord blood showed a positive correlation with TSH levels (r=0.39, p=0.001). No significant correlations were observed between the other metals and hormone levels in the cord blood as well as in the maternal plasma. Lead concentration was associated with higher weight at 12 months (r=0.287, p=0.007) and greater weight gain from the 3rd to 12th month (r=0.305, p=0.006). Conversely, Arsenic showed a negative correlation with weight gain from the 6th to the 12th month (r=-0.238, p=0.042).

Conclusions:
Prenatal arsenic exposure may be associated with alterations in TSH levels in umbilical cord blood.
Furthermore, both lead and arsenic appear to induce changes in weight gain during the first year of life.

Funding:
FAPERJ, CNPq, CAPES, INCT.

Key-words: (up to 5):
endocrine-disrupting chemicals; thyroid; heavy metals; mother; infants.

Abstract #00006732 en

Characterization of micronutrient intake from the NOVA classified foods and supplements among Brazilian children aged 6 to 59 months (ENANI-2019)

Public Health Policies Across the Life Cycle.

Nascimento dos Santos Isabel (1), Castro Inês Rugani Ribeiro de (2), Normando Paula (1), Sousa Taciana Maia de (2), Carneiro Letícia Barroso Vertulli (3), Machado Raquel Schincaglia (4), Kac Gilberto (1)
(1) Institute of Nutrition Josué de Castro, Federal University of Rio de Janeiro, (2) Institute of Nutrition, State University of Rio de Janeiro, (3) Institute of Collective Health Studies, Federal University of Rio de Janeiro, (4) Faculty of Nutrition, Federal University of Goias

Background/aims:
Micronutrient deficiencies among children remain a global public health challenge, which reinforces the need to ensure a sufficient supply of micronutrients for this group. This study describes the intake of micronutrients from food and supplements among children aged 6–59 months from the Brazilian National Survey on Child Nutrition (ENANI-2019).

Methods:
The intake of vitamin A, vitamin B12, iron, and zinc was estimated using a 24-hour dietary recall and a questionnaire about micronutrient supplement intake at the time of the interview, based on data from ENANI-2019, a national household survey. Medians and 95% confidence intervals of micronutrient intake were calculated according to the Nova food classification groups (G1-3: unprocessed or minimally processed foods, processed culinary ingredients, breast milk; and G4: ultra-processed foods) and supplement use. The study was approved by the ethics committee (CAAE 89798718.7.0000.5257), and all participants provided informed consent.

Results:
The median intake of vitamin A, vitamin B12, and zinc from G1–G3 food sources exceeded the Estimated Average Requirement (EAR), even among socioeconomically vulnerable children. In contrast, iron intake from these sources was below the EAR for children <1 year of age (y). Among supplement users, the median of total iron intake from G1-G3 food sources plus supplements exceeded the EAR and G4 foods made a significant contribution to vitamin A, iron, and zinc intake. However, total median intake of vitamin A and zinc exceeded the Tolerable Upper Intake Level (UL).

Conclusions:
The Brazilian Ministry of Health's strategies, aimed at preventing iron deficiency among children <2 y through prophylactic supplementation, combined with promoting iron-rich foods for groups G1–3, are justifiable. Consuming foods from group G4, along with the use of supplements, may result in intakes exceeding the UL for zinc and vitamin A.

Funding:
Brazilian Ministry of Health / Brazilian National Research Council (CNPq)

Key-words: (up to 5):
Dietary Supplements; Preschool children; Micronutrient intake

Abstract #00006738 en

Neonatal maternal overnutrition induces sex-related metabolic and reproductive changes in adult offspring

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Guergolette Rhauany (1), Lopes Gabriela (1), Stopa Larissa (1), Oliveira Maria Heloisa (1), Souza Camila (1), Martins Andressa (1), Gerardin Daniela (1), Quadreli Debora (1), Fernandes Glaura (1), Andrade Fabio (1), Zaia Dimas (1),
Zaia Cassia Thais (1), Leite Cristiane (1), Uchoa Ernane (1)
(1) Universidade Estadual de Londrina (UEL)

Background/aims:
A classic model to induce early overnutrition is litter size reduction, which increases milk availability and leads to overfeeding. For this, on postnatal day (PND) 3, the litter size is adjusted for 3 pups (2 males and 1 female), forming the small litter (SL), or for 10 pups (5 males and 5 females), forming the normal litter (NL). SL females exhibit metabolic changes associated with reproductive dysfunctions, and neonatal overfeeding in females predisposes the development of obesity in their male offspring.

Methods:
This study evaluated reproductive and metabolic changes in the offspring of female Wistar rats exposed to postnatal overnutrition by litter size reduction. For this, after weaning (PND21), food intake and body weight were evaluated until PND60. Vaginal opening, first estrus, coefficient of each phase of the estrous cycle, the onset of the estrous cyclicity, and the preputial separation were evaluated. On PND59, animals were subjected to a Glucose Tolerance Test (GTT), and on PND60, the Lee index was calculated, and the animals were euthanized by decapitation.

Results:
Male offspring of SL mothers presented higher body weight, glucose intolerance, increased adiposity and plasma triglyceride levels, earlier preputial separation, reduced testosterone levels, decreased number of Leydig and Sertoli cells, increased prevalence of abnormal seminiferous tubules, diameter and height of seminiferous tubules, higher proportion of immature germ cells within the seminiferous lumen, and altered proportions of the stages of spermatogenesis. Female offspring of SL mothers showed elevated free fatty acid levels and adiposity, reduced estradiol levels, delayed onset of the estrous cyclicity, increased prevalence of diestrus stages I and II, and diminished primordial ovarian follicles.

Conclusions:
The present study showed offspring of SL mothers present reproductive and metabolic dysfunctions; however, these impairments are more evident in males, indicating a sexual dimorphism in the outcomes in the offspring of mothers with early obesity.

Funding:
CAPES, Fundação Araucária-PR and CNPq.

Key-words: (up to 5):
preconception, maternal nutrition, metabolic syndrome, DOHaD, litter size reduction

Abstract #00006739 en

Association between human milk and cow's milk intake and the serum metabolome of Brazilian children aged 6–24 months: Brazilian National Survey on Child Nutrition (ENANI-2019)

Role of Infant and Young Child Feeding Practices on Long-Term Health

Oliveira Driele Rodrigues (1), Campos Adriana Divina de Souza (1), Freire Samary da Silva Rosa (1), Normando Paula (1), Castro Inês Rugani Ribeiro de (2), Schincaglia Raquel Machado (3), Vicente Lucas Goldenberg (1), Kroezen Zachary (4), Shanmuganathan Meera (4), Britz McKibbin Philip (4), Kac Gilberto (1)
(1) Nutritional Epidemiology Observatory, Federal University of Rio de Janeiro, (2) Institute of Nutrition, State University of Rio de Janeiro, (3) Faculty of Nutrition, Federal University of Goiás, (4) Department of Chemistry and Chemical Biology, McMaster University

Background/aims:
Early-life feeding practices, such as breastfeeding and introduction of cow's milk, play a critical role in metabolic phenotype during infancy. This study investigated the association between human and cow's milk intake and serum metabolomic profiles in Brazilian children aged 6–24 months.

Methods:
Methods: Data from 1562 children aged 6–24 months were obtained from the Brazilian National Survey on Child Nutrition (ENANI-2019). Milk intake was categorized as human milk (HM), cow's milk (CM), both (HC), and no milk (NM). Untargeted metabolomics analysis was performed, and 75 polar/ionic metabolites were assessed using multisegment injection-capillary electrophoresis-mass spectrometry. Associations between milk intake and metabolite concentrations were assessed using linear regression models adjusted for child's age, sex, region, socioeconomic status, and BMI z-score. Metabolites were scaled. Pairwise comparisons used estimated marginal means with false discovery rate correction. $P < 0.05$ was significant. Ethical approval was obtained (CAAE 89798718.7.0000.5257), and informed consent was provided by caregivers.

Results:
Significant differences in serum tyrosine and valine concentrations were observed among feeding groups. Children in the CM group had significantly higher tyrosine compared to NM ($\beta = –0.33$, $p = 0.01$), HM ($\beta = 0.57$, $p < 0.01$), and HC ($\beta = 0.33$, $p < 0.01$). Similarly, valine concentrations were higher in CM compared to NM ($\beta = –0.30$, $p = 0.01$), HM ($\beta = 0.56$, $p < 0.01$), and HC ($\beta = 0.32$, $p < 0.01$). Additional comparisons showed HM also had higher tyrosine and valine than HC (both $p < 0.01$), while no significant difference was observed between NM and HC.

Conclusions:
Early dietary protein sources, particularly cow's milk, may influence serum tyrosine and valine concentrations in the first two years. Further research is warranted to better understand how infant feeding patterns impact metabolic outcomes.

Funding:
Brazilian Ministry of Health/ Brazilian National Research Council (CNPq).

Key-words: (up to 5):
Breastfeeding, Metabolomics, Infant, Nutrition, Amino Acids

Abstract #00006740 en

Maternal High-Sugar Diet Induces Sex-Dimorphic Pancreatic Alterations In Early Adult Offspring

Impact of Preconceptional Health and Lifestyles on Offspring Health Throughout the Life Cycle

Barbosa Rafael (1), Fernández Arturo (1), Macedo Bruno (2), Pontes Jaqueline (2), Brito Camila (2), Silva Odara (2), Sanches Jonas (2), Freitas Perla (2), Flister Karla (2), França Lucas (2), Pinto Bruno (2), Coelho Caio Fernando (2),
Paes Antonio Marcus (2)
(1) UNDB, (2) UFMA

Background/aims:
Higher levels of simple carbohydrates consumption during pregnancy and lactation have been associated to metabolic outcomes in offspring, mostly during early adulthood. Thus, this study investigated the impacts related to a high-sucrose diet (HSD) exposure in the offspring of rats midst the perigestacional stage, centering on pancreatic morphology.

Methods:
Female Wistar rats were fed with isocaloric HSD (25% sucrose) or regular chow (10% sucrose, CTR) for a total period of 12 weeks. Male and female offspring were fed regular chow from weaning until euthanasia at 30 days old, when blood and pancreas were collected (CEUA/UFMA no 23115.0002915/2023-62). Pancreatic tail was processed for hematoxylin&eosin staining and images were analyzed through ImageJ software.

Results:
HSD offspring (HSDF females; HSDM males) were not weighter. However, they presented metabolic syndrome features in a sexual dimorphic way. HSDF developed hyperglycemia, whereas HSDM exhibited hypertriglyceridemia and peripheral insulin resistance, assessed by TyG index. In like manner, pancreas morphology changed in a dimorphic way in HSD offspring. HSDF pancreas were weighter and had more total area of islets in their tail (CTRF=0,6500 ± 0,1609% of total area vs. HSDF=1,746±0,1513% of total area). Moreover, pancreatic islets from HSDF were hyperplasic and hypertrophic: larger area (CTRF=640.740±93.212 µm2 vs. HSDF=1.253.716±114.768 µm2), higher cellularity (CTRF=105,2±17,68 vs. HSDF=155,8±17.02) and larger cellular mean area (CTRF=6.810±369,3 µm2 vs. HSDF=8.489±173,8 µm2). Differently, HSDM pancreas presented lower cellularity in their islets (CTRM=154,3±13,08 vs.
HSDM=191,0±23.24), with no other morphological changes.

Conclusions:
Our findings arise sex-specific differences in the development of metabolic syndrome, where females are more prone to hyperglycemia and males to dyslipidemia. These outcomes are partially explained by pancreatic morphological changes. In addition, these results reveal clear sexual dimorphism regarding metabolic outcomes from intergenerational transmission of programmed effects.

Funding:
CNPq, CAPES and FAPEMA.

Key-words: (up to 5):
Added sugars; Fetal programming; Pancreatic islets; Metabolic syndrome; Diabetes.

Abstract #00006741 en

Obesity induced by lactation overnutrition induces oxidative stress and metabolic impairments in skeletal muscles and liver of male Wistar rats

Role of Infant and Young Child Feeding Practices on Long-Term Health

Stopa Larissa (1), Guergolette Rhauany (1), Aguiar Danielly (1), Shishido Polyana (1), Erthal Rafaela (2), Bertozzi Mariana (1), Tenorio Pedro (1), Andrade Fabio (1), Zaia Cassia Thais (1), Fernandes Glaura (1), Verri Jr Waldiceu (1), Leite Cristiane (3), Uchoa Ernane (1)
(1) Universidade Estadual de Londrina (UEL), (2) Universidade Federal do Paraná (UFPR), (3) Universidade Estadual de Londrina

Background/aims:
The early years are marked by neuroendocrine plasticity, making the organism particularly susceptible to metabolic programming. Excessive body weight in the early stages of life notably increases the risk of obesity in adulthood. Obesity is associated with oxidative stress and chronic low-grade inflammation, and also with cardiovascular risk, dyslipidemia, insulin resistance, type 2 diabetes mellitus, liver disease, among other harms to physical health.

Methods:
This work aimed to evaluate the consequences of obesity induced by lactational overnutrition on energy homeostasis and the redox and inflammatory status in the main tissues involved in its regulation, in young adult male rats. Animals were assessed until postnatal day (PND) 60, comparing those from normal litters (NL) and small litters (SL).

Results:
On PND 60, the SL group exhibited increased body weight and adiposity, characterized by adipocyte hypertrophy, despite reduced food intake, and the presence of glucose intolerance and increased insulin plasma levels. Additionally, the liver of SL animals displayed signs of oxidative damage and elevated levels of the pro-inflammatory cytokine IL-1β. In the SL group, the soleus muscle also showed increased content of glucose and lipid peroxidation, and the gastrocnemius muscle exhibited increased reactive oxygen species. The liver and the muscles of SL presented enhanced lipid accumulation, whereas plasma concentrations of triacylglycerols were decreased.

Conclusions:
In conclusion, given that these tissues are crucial for regulating glycemic metabolism, the observed oxidative stress may have contributed to the onset of glucose intolerance in animals with childhood obesity during early adulthood, likely by impairing muscle glucose utilization.

Funding:
CAPES, CNPq and Fundação Araucária-PR.

Key-words: (up to 5):
Lactation Overnutrition, DOHaD, Oxidative Stress, Energy Homeostasis

Abstract #00006744 en

Lactation overnutrition-induced adiposity is associated with a reduced lipolytic pathway in white adipose tissues: modulation by glucocorticoids

Interventional strategies to prevent late-life outcomes resulting from early-life insults

Souza Camila (1), Stopa Larissa (1), Martins Andressa (1), Wunderlich Ana Luiza (1), Lopes Gabriela (1), Silva Flaviane (2), Komino Ayumi (2), Andrade Fabio (1), Lima Fabio (2), Zaia Cassia Thais (1), Leite Cristiane (1), Uchoa Ernane (1) (1) Universidade Estadual de Londrina (UEL), (2) Universidade de São Paulo (USP)

Background/aims:
Lactation overnutrition induced by litter size reduction leads to the early onset of obesity, which persists into adulthood. Elevated levels of circulating glucocorticoids, increased adiposity and insulin resistance are observed disruptions in this obesity model. Bilateral adrenalectomy (ADX) has been shown to contribute to comorbidities in various obesity models. Thus, this study assessed the lipolytic and insulin signaling pathways in white adipose tissues, and their regulation by glucocorticoids in adult rats with lactation overnutrition.

Methods:
Adult male rats reared from small litter (SL) or normal litter (NL) underwent bilateral adrenalectomy (ADX) or sham surgery, and half of the ADX animals received corticosterone (CORT- 25 mg/L). On PDN 74, animals were submitted to euthanasia by decapitation, and retroperitoneal and epididymal adipose tissues were removed, weighed, and stored for subsequent histological and western blotting analyses.

Results:
SL rats exhibited increased body weight gain, weight and adipocyte area in both fat depots, along with glucose intolerance. SL animals also showed a reduction in the protein expression involved in lipolysis, particularly in the retroperitoneal fat depot, with no changes in the insulin signaling pathway in both fat depots. ADX decreased body weight gain, and adiposity in both fat depots, as well as improved glucose intolerance in SL rats. However, ADX did not alter the lipolytic pathway changes. CORT reversed most of the parameters changed by ADX, without affecting the changes induced by SL in lipolytic protein expression.

Conclusions:
In summary, this study suggests that circulating glucocorticoids likely contribute to the increased adiposity and glucose intolerance induced by lactational overnutrition in male rats. However, the observed effects seem not to involve the lipolytic and insulin signaling pathways of retroperitoneal and epididymal fat depots.

Funding:
CAPES, CNPq and Fundação Araucária

Key-words: (up to 5):
adrenalectomy, litter size reduction, lipolysis, obesity, glucose intolerance

Abstract #00006745 en

The impact of Family Policies Expenditure on total fertility rates. A Panel Data Analysis of OECD Countries

Public Health Policies Across the Life Cycle.

Donoso Manuel (1), Mardones Francisco (2), Arévalo Isidora (3), Donoso-Mena Magdalena (4), Fluxá María Teresa (4), Guarello Sofia (4), Larraín José Ignacio (4), Croxatto Paloma (4), Sepúlveda Alejandro (5)
(1) Department of Obstetrics, Gynecology and Reproductive Biology, Universidad de los Andes , (2) Pontificia Universidad Católica de Chile, (3) Facultad de Medicina, Universidad de los Andes, (4) Faculty of Medicine, Universidad de los Andes, (5) Department of Epidemiology

Background/aims:
The total fertility rate (TFR) is the number of children a woman will have throughout her reproductive life. The population replacement rate is 2.1 children per woman. The TFR has fallen dramatically in recent decades. The TFR in 2021 was estimated at 2.23, and the projection for 2050 is 1.83. Each country has family-related public policies (FP) that impact the TFR. Each FP group has a cost equivalent to a percentage of the gross domestic product (GDP). Our objective was to evaluate the relationship between a country's spending on FP as a percentage of GDP and the TFR over time in member countries of the Organization for Economic Cooperation and Development (OECD).

Methods:
A longitudinal cross-country panel data study was conducted using OECD public-use databases that include GDP expenditure data on family policies and TFR from 1995 to 2021 across the 38 OECD member countries. The OECD divides family policies into cash, services, and taxes policies. Linear mixed models (LMMs) were used to analyze the longitudinal relationships between variables over time. Survival analysis with a Cox model and logistic models with random effects were used to determine a country's risk of having a TFR <1.6 over time.

Results:
Higher total and services GDP are positively associated with higher TFRs over time. Investment in family policies >2% of GDP decreases the risk of a country having a TFR <1.6 by 51% (HR=0.49 (0.24-0.99)(p<0.046)), and one standard deviation of service expenditure reduces the same risk by 34% (HR=0.66 (0.45, 0.98)(p<0.040)). Logistic models confirm these findings.

Conclusions:
A GDP >2% in FP and higher spending on services, mainly childcare for children under 5 years of age, are associated with better TFRs and prevent a country from decreasing its TFR <1.6 in OECD member countries

Funding: none

Key-words: (up to 5):
total fertility rate, family policies, gross domestic product, OECD, Demography