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In This Issue

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This issue of the General Developmental Origins of Health and Disease contains one review article, 11 original papers, and 4 brief reports. The review article emphasizes the impact of maternal exposures on human milk composition, emphasizing the increasing evidence of marked variation in the nearly 200 component within milk. Altered milk composition may have significant impact on newborn growth and development.

Review articles

Non-nutritive bioactive components in maternal milk and offspring development: a scoping review. Eisha and colleagues utilized a scoping review of 40 primary research articles to identify maternal nutritional, psychosocial and environmental exposures which may influence non-nutritive bioactive factors milk composition. Among the factors, the results demonstrate that maternal obesity influences milk hormones, microRNAs and inflammatory cytokines. These milk components may have important consequences on offspring developmental outcome.

Original Articles

Adulthood asthma as a consequence of childhood adversity: A systematic review of epigenetically affected genes. Saygideger et al utilized asthma as representative of a chronic disease that may be influenced by genetic regulation of inflammatory biomolecules. The authors hypothesize that childhood adversity may alter epigenetic regulation of asthma related genes. Utilizing a systematic review the authors determined that several genes and pathways contributing to pathogenesis of asthma are epigenetically affected by childhood trauma. These findings add to the importance of the recognition and prevention of childhood adversity and trauma.

Defining the role of the hypothalamic-pituitary-adrenal axis in the relationship between fetal growth and adult cardiometabolic outcomes. Martin and coauthors utilized the Raine Study cohort to examine the role of the HPA-A axis in fetal growth and adult cardiometabolic outcome. The results demonstrated a linear relationship between fetal growth and BMI in young adults. However HPA-A function did not modify the relationship. The authors conclude that their data does not that HPA-A function in young adulthood mediates the relationship between fetal growth and cardiometabolic risk.

Hyperglycemia in pregnancy and developmental outcomes in children at 18-60 months of age: The PANDORA Wave 1 study. Titmuss et al explored the association between hyperglycemia in pregnancy and child development in a longitudinal birth cohort from Australia. Maternal hyperglycemia was associated with increased developmental “concern” in fine motor and problem solving domains among offspring. The authors suggest that maternal hyperglycemia may be a potential intervention target to optimize developmental outcomes.

Aberrant inflammation in rat pregnancy leads to cardiometabolic alterations in their offspring and intrauterine growth restriction in the F2 generation. Ushida and coauthors examined F1 and F2 offspring of dams exposed to LPS during pregnancy. F1 offspring demonstrated gender specific alterations in blood pressure, glucose tolerance, and body composition, whereas F2 offspring demonstrated reductions in fetal growth. These findings demonstrate the transgenerational impact of abnormal maternal inflammation and may have relevance to human pregnancy conditions including preeclampsia.

Limosilactobacillus fermentum prevent gut-kidney oxidative damage and the rise in blood pressure in male rat offspring exposed to a maternal high fat diet. do Nascimento et al examined the effect of daily *Limosilactobacillus fermentum* supplementation to dams fed a high fat diet during pregnancy and lactation. The addition of the probiotic strain was associated with reduced blood pressure and improved renal function in male offspring from dams fed the high fat diet. The authors postulate a beneficial mechanism through via oxidative stress modulation.

Dipeptidyl peptidase IV inhibition delays developmental programming of obesity in metabolic disease in male offspring of obese mothers. Montaniel et al proposed that DPP IV, an adipokine, may contribute to offspring weight gain and altered metabolism. The authors confirmed increased maternal and cord blood DPP IV activity in human male offspring and offspring of obese nonhuman primate mothers. In a mouse model of maternal high fat diet induced obesity, a DPP IV inhibitor administered to mothers prior to and throughout pregnancy and lactation delayed the progression of obesity and metabolic disease in male offspring. These findings suggest a potential role of the DPP IV in the transgenerational propagation of obesity.

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Protective effect of antioxidants on cardiac function in adult offspring exposed to prenatal overnutrition. Zhang and coauthors examined mice offspring exposed to maternal obesity, demonstrating consequences of increased oxidative stress in myocardial tissue. The administration of N-Acetyl Cysteine during pregnancy reduced the impact of oxidative stress and altered offspring cardiac abnormalities. These findings suggest that potential target for the prevention of offspring cardiovascular disease resulting from fetal overnutrition.

The effect of wasting and stunting during severe acute malnutrition in infancy on insulin sensitivity and insulin clearance in adult life. Thompson and coauthors examined 40 adult severe acute malnutrition survivors for measures of insulin sensitivity and clearance. Survivors with both marasmus and kwashiorkor had similar body composition and both groups had similar glucose disposal rate and insulin clearance as compared to controls. These findings suggest that wasting and stunting during infancy is not associated with altered insulin sensitivity and insulin clearance. Rather malnutrition survivors may have glucose intolerance as a result of beta cell dysfunction.

Gestational weight gain is associated with childhood height, weight and BMI in the Peri/Postnatal Epigenetic Twins Study. Ashtree and coauthors utilized the PETS prospective cohort study of twins to examine the association of gestational weight gain with twin weight, height and BMI to age six. The results demonstrate that gestational weight gain was associated with twin length, weight and BMI at birth, but the effects did not persist through childhood.

Are there sex differences in fetal growth strategies and in the long term effects of pregnancy complications on cognitive functioning? Christians and Chow utilized data from the National Collaborative Perinatal Project to examine sex differences in growth and cognitive function. Being born small for gestational age or very preterm was associated with reduced cognitive performance, with select sex specific effects. The authors discussed the potential spurious effects of analyzing sex dependent effects in the absence of significance for interaction.

A prospective cohort study of head circumference and its association with neurodevelopmental outcomes in infants and young children in rural Guatemala. Connery and coauthors examined head circumference in a lower income country environment. The results indicate that children with smaller head circumference do less well on developmental tests through one year

of age. The authors suggest that head circumference measures should be considered for inclusion in developmental screening assessments.

Brief reports

Twins in Guinea-Bissau have a “thin fat” body composition compared to singletons. Wagh and coauthors performed an analysis of body composition of twins and singletons in Guinea-Bissau. Twins had lower birth weight and at followup (age 7-34 years) lower height, weight and BMI compared to singletons, but higher adiposity. These results suggest that a thin fat phenotype in twins of a low socioeconomic African country may be a manifestation of early life undernutrition.

Intergenerational effects of prenatal hypoxia exposure on uterine artery adaptations to pregnancies in the female offspring. Wooldridge and coauthors studied rat offspring exposed to prenatal hypoxia between day 15 to 21 of gestation. Pregnant adult offspring who had been exposed to prenatal hypoxia demonstrated reduced placental weight and increased uterine artery circumferential stress. These results suggest an intergenerational effect of prenatal hypoxia.

Impact of COVID-19 pandemic on research and careers of early career researchers: A DOHaD perspective. Bansal and colleagues assessed the potential impact of COVID-19 pandemic reporting a marked impact on daily research activities and career development plans among early career researchers. These findings emphasize the importance of supporting early career researchers as a consequence of the COVID-19 epidemic.

Circulating microRNAs from early childhood in adolescence are associated with pre-diabetes at 18 years of age in women from the PMNS cohort. Joglekar and colleagues studied women from the Pune PMNS birth cohort.

The results suggested select circulating microRNAs assessed over early life may be predictive of prediabetes at 18 years of age.

Letter to editor regarding “cardiovascular risk factors in offspring exposed to gestational diabetes mellitus in utero: Systematic review in meta-analysis.”

Author Responses:

Erratum:

Sincerely,

Michael G. Ross, MD, MPH
Editor-in-Chief