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In This Issue

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This issue of the Developmental Origins of Health and Disease has 17 articles including two review articles, two brief reports, and 13 original manuscripts. Notably, two articles examine the concept that maternal hormone activity during early pregnancy may impact offspring health and disease. These two studies fail to find a relationship between digit ratio and early steroid exposure, suggesting that digit ratio may not be a simple marker of fetal hormone exposure.

Review Articles

Selecting life course frameworks to guide and communicate large new cohort studies: Generation Victoria (GenV) case study. Wang et al provide an assessment as to how to select publicly available frameworks for planning and communicating early life cohort studies. The authors demonstrate how they selected the one life course framework, hence the GenV primary framework. This approach will be of value to investigators planning cohort studies.

Season-of-birth phenomenon in health and longevity: Epidemiologic evidence and mechanistic considerations. Vaiserman evaluates the research evidence for seasonality of birth in DOHaD-related disorders. Factors relevant to prenatal and neonatal development include nutrition, outdoor temperature, infectious exposures, and duration of sunlight, among others. The author discusses potential mechanisms underlying the impact of seasonal programming upon chronic disease and longevity.

Brief Reports

Digit ratio (2D:4D) and amniotic testosterone and estradiol: An attempted replication of Lutchmaya et al. Richards and colleagues attempt to replicate the report of Lutchmaya from 2004 who demonstrated the ratio of testosterone to estradiol in second trimester amniotic fluid was negatively correlated with digit ratios for the right hand. The prospective study with four-and-a-half-year follow-up did not demonstrate a correlation between the hormone markers and digit ratios, raising the question as to the prior premise that second trimester sex hormones affect the development of digit length.

Gestational exposure to Δ^9-THC impacts ovarian follicular dynamics and angiogenesis in adulthood in Wistar rats. Martinez-Pena and co-authors examine the effects of prenatal Δ^9-THC on ovarian health. At six months of age, THC-exposed offspring had accelerated folliculogenesis with apparent follicular development arrest. The offspring had decreased expression of VEGF and its receptor VEGF-2, suggesting that Δ^9-THC exposure during pregnancy alters follicular dynamics during postnatal life and may have detrimental long-term effects on female reproductive health.

Original Articles

Leptin administration during lactation leads to different nutritional, biometric, hemodynamic, and cardiac outcomes in preubertal and adult female Wistar rats. de Souza et al administered leptin to female rats for the first 10 days of lactation. The leptin offspring demonstrated lower food intake between PMD 21 and 30 and altered echocardiographic measurements at PMD 30. These findings suggest a variety of nutritional and cardiac effects due to neonatal leptin administration that illustrate developmental plasticity.

Associations between stool micro-transcriptome, gut microbiota, and infant growth. Carney and colleagues hypothesized that infant stool miRNAs would be associated with microbial activity and infant growth. The authors found that increased RNA transcriptional activity of *Clostridia* and *Burkholderia* was associated with infant growth with a likely target of four metabolic pathways. These findings suggest that these molecules may regulate the biosynthetic landscape of the gut and provide further evidence for the importance of the infant microbiome.

First 1,000 days: New Zealand mothers' perceptions of early life nutrition resources. Hildreth and co-authors assess first-time New Zealand mothers' perceptions of evidence-based dietary guidelines for the first 1,000 days. The authors report that mothers related to the booklet depending upon level of their health literacy, tendency to outsource decision-making, and pressure to comply. The authors provide suggestions for development of resources for nutrition guidelines that would improve their efficacy.

Caregiving adversity during infancy and preschool cognitive function: Adaptations to context? Rifkin-Graboi and colleagues examine maternal sensitivity in infancy and offspring cognitive performance three years later. Maternal sensitivity in infancy was highly predictive

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of worse memory for socioemotional stimuli and predictive of better memory when nonsocioemotional stimuli were used. The authors describe how an adaptation-to-context framework may aid in designing pedagogical strategies and well-being interventions.

Hair cortisol levels in pregnancy as a possible determinant of fetal sex: A longitudinal study. Romero-Gonzalez et al assess the relationship between the sex of the offspring and the stress of the mother during the first trimester of pregnancy as quantified by hair cortisol levels. The concentration of cortisol was higher if the baby was a girl than boy, suggesting that the sex of the future baby could be conditioned by the mother's stress levels during conception and first weeks of pregnancy.

Placental adaptations in a nonhuman primate model of gestational protein restriction. Roberts and co-authors hypothesize that a protein-restricted diet prior to and throughout pregnancy would impair placental taurine uptake in Rhesus macaques. The authors demonstrate conserved fetal growth despite a decrease in placental taurine uptake in response to the protein-restricted diet. Expansion of the syncytiotrophoblast surface area may be one compensatory mechanism by the placenta to maintain fetal growth.

The impact of maternal protein restriction during perinatal life on the response to a septic insult in adult rats. Khazaee et al utilize a model growth-restricted fetal rats resulting from maternal protein-restricted diet who were subsequently exposed to a postnatal intraperitoneal septic infection. Fetal growth restriction did not impact liver or lung inflammatory responses to sepsis in either male or female adult offspring, but did alter the relative amount of surfactant in male growth-restricted offspring. This altered septic response in male offspring may imply a contribution to lung dysfunction.

Digit ratio, proposed marker of the prenatal hormone environment, is not associated with prenatal sex steroids, anogenital distance, or gender-typed play behavior in preschool-age children. Barrett assesses sex difference in digit ratio in relation to child sex, maternal sex steroid hormone concentrations in early pregnancy, anogenital distance, and gender-typical play at age 4. The authors observe no evidence that early childhood digit ratio is associated with child sex or hormone-sensitive measures. The authors discuss challenges in assessing fetal hormone exposure.

Nutrition between the first 1,000 days: Diet quality and 7-year change in BMI in overweight 3-year-old children from the Dutch GECKO Drenthe birth cohort. Vinke and colleagues assess the association between diet quality of children aged 3 years and change in BMI in the following seven years. Children with a poor diet quality at age 3 had a considerably higher risk for overweight at age 10. These findings emphasize the lifelong importance of early dietary habits and the opportunity for early life preventative strategies.

Sex- and age-dependent differences in nicotine susceptibility evoked by developmental exposure to tobacco smoke and/or ethanol in mice. Nunez-Freitas and co-authors assess whether short-term ethanol exposure, when combined with chronic exposure to tobacco smoke, aggravates susceptibility to nicotine in adolescent and adult mice. The results indicate that ethanol exposure during the brain growth spurt, when combined with developmental exposure to tobacco smoke, increases nicotine susceptibility with a stronger effect in adult females. The findings suggest that early developmental dual exposure may predispose to nicotine use/abuse later in life.

Epigenetic mechanisms involved in intrauterine growth restriction and aberrant kidney development and function. Doan et al examine the epigenetic mechanisms by which growth-restricted rats have significant nephron deficits. The authors demonstrated sex-specific differences in imprinted genes among the growth-restricted males as compared to females. Their results delineate potential epigenetic mechanisms that may alter renal embryonic and/or fetal development.

PPARγ activation in late gestation does not promote surfactant maturation in the fetal sheep lung. Ren and co-authors examine the effects of continuous fetal administration of the PPARγ agonist or leptin on surfactant protein maturation. Leptin infusion significantly increased the expression of PPARγ and IGF-2, though the expression of the majority of genes involved in surfactant synthesis was not affected. These results suggest a potential decreased capacity for surfactant phospholipid and protein production in the fetal lung in response to PPAR agonists and/or leptin administration.

Renal morphology and glomerular capillarization in young adult sheep born moderately preterm. Sutherland et al examine the long-term impact of preterm birth on renal morphology in sheep born moderately preterm. By 14.5 months of age, there was no difference between preterm and term sheep in body or kidney length, though renal corpuscle volume was significantly larger in preterm sheep. These findings suggest that moderate preterm birth does not adversely affect glomerular structure in early adulthood.

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