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In This Issue

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This issue of Developmental Origins of Health and Disease contains 14 original articles and two excellent reviews. In our Mini-Theme Issue, four studies focus on reproductive effects of early life exposures, including androgen effects on male spermatogenesis and hippocampal development, and estrogen and endocrine disrupter impact on female uterine and ovarian morphology.

Review Articles

Respiratory viral infections during pregnancy: Effects of SARS-CoV-2 and other related viruses over the offspring. Riedel and co-authors discuss the impact of SARS-CoV-2 in pregnant patients including immune effects, fetal growth, pregnancy viability and neonatal morbidity.

COVID-19: Can we treat the mother without harming her baby? Wiese and co-authors discuss the dilemma of vaccine and drug trials and treatments for pregnant women in regard to both maternal and fetal effects. The authors acknowledge that pregnant women are especially vulnerable to the effects of COVID-19, yet there is limited guidance on drug treatment for pregnant women with severe symptoms.

Mini-Theme Issue

Reproductive Effects of Early Life Exposures

High-fructose diet during puberty alters the sperm parameters, testosterone concentration and histopathology of testes and epididymis in adult Wistar rats. Medaglia et al evaluated reproductive effects of high-fructose diet in male Wistar rats. Fructose diet induced an increase in abnormal seminiferous tubules and luminal changes, coinciding with altered spermatogenesis and sperm production. These findings demonstrate the potential impact of high-fructose diet on offspring male fertility.

Role of testosterone:cortisol ratio in age- and sex-specific cortico-hippocampal development and cognitive performance. Caccese et al examined the association among testosterone:cortisol ratio, cortico-hippocampal structure and standardized test responses in a cohort of children and adolescents. Greater testosterone to cortisol ratios were associated with greater coordinated growth between the hippocampus and cortical thickness, which were related to lower verbal/executive function though greater attention in tests of visual spatial abilities.

Prolonged atrazine exposure beginning *in utero* and adult uterine morphology in mice. Griffiths and colleagues examined the uterine effect of atrazine, an herbicide that acts as endocrine disruptor. Pregnant mice were exposed to atrazine during the second half of gestation through weaning. The authors reported endometrial hyperplasia and leiomyoma in atrazine-exposed mice, indicating that exposure may negatively affect female fertility.

Prenatal and pubertal exposure to 17-alpha ethinyl estradiol disrupts follicular genesis and promotes morphophysiological changes in ovaries of old gerbils. DeSouza et al examined the effects of low-dose ethinyl estradiol in ovaries from 12-month-old gerbils with exposure varied between early and late gestation. The results indicate that exposure to ethinyl estradiol during prenatal and pubertal periods lead to morphologic changes in senile ovaries.

Original Articles

Gut lumen formation defect can cause intestinal atresia: Evidence from histological studies of human embryos and intestinal atresia septum. Liu and co-authors performed histological studies on six- to 10-week gestation human embryos demonstrating the formation of the gut lumen. The authors propose a mechanism by which a perturbation of the fusion of vacuoles with the intestinal wall could lead to intestinal atresia.

The fetal origins of disease: A prospective cohort study on the association of preeclampsia and childhood obesity. Palma dos Reis and colleagues analyzed the association between preeclampsia and childhood obesity in 5133 women/children pairs assessed at 10 years of age. Offspring of preeclamptic mothers had a higher BMI though the association was not statistically significant. The authors conclude that confounding variables, including maternal BMI, parity and smoking, are important contributory factors to childhood obesity.

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Prenatal programming of depression: Cumulative risk or mismatch in the Ontario Child Health Study? Savoy and Van Lieshout examined a retrospective cohort from the Ontario Child Health Study to assess the association between birth weight status, childhood stress and depression in adulthood. The authors suggest that mental health of adults born low birth weight may be more resilient to the adverse effects of childhood/adolescent stress, implying a mismatch of gestational and early life stress.

Cardiovascular risk factors in extended family members and birth weight in offspring. Shaikh et al investigated the association between offspring birth weight and cardiovascular risk factors among extended family members from Norway. The authors indicate that the associations go beyond the expected genetic similarities suggesting that mechanisms, including environmental factors, assortative mating and genetic nurturing, may explain the associations.

Late effects of early weaning on food preference and the dopaminergic and endocannabinoid systems in male and female rats. Soares and co-authors studied the effect of early weaning (three days) on offspring food preference as adults. The results indicate that early weaning altered both dopaminergic and endocannabinoid systems in select brain regions contributing to altered dietary preferences.

A model of optimal timing for predictive adaptive response. Spencer et al discuss how predictive adaptive responses are a form of developmental plasticity. The authors suggest that predictive adaptive responses will evolve under three circumstances related to timing constraints on cue and environmental status, and suggest these predictions are empirically testable.

Association of chemerin gene promoter methylation in maternal blood and breast milk during gestational diabetes. Fatima and colleagues examined methylation of chemerin, a placental-produced protein with chemoattractive properties. Maternal serum and chemerin levels at 28 weeks were lower for normal glycemic mothers as compared to gestational diabetes (GDM) mothers. Forty percent of GDM mothers expressed unmethylated chemerin reflecting increased chemerin concentration in

the maternal blood. These studies suggest the critical role of methylation in regulating protein expression during diabetic pregnancies.

Maternal hepatitis B or C carrier status and long-term risks for offspring neurological morbidity: A population-based cohort study. Yoles and colleagues examined long-term childhood neurological morbidity in offspring born to HBV/HCV carrier mothers. The cumulative incidence of neurological hospitalizations was higher in children born to carrier mothers and remained higher after adjusted for gestational age and pregnancy complications. The authors suggest that mechanisms including microbiome alterations, immune system modulations or epigenetic changes may impact on offspring long-term health.

Body composition during the first four month in infants affected by neonatal abstinence syndrome: A pilot study. Corr and colleagues measured infant body composition in newborns with neonatal abstinence syndrome. Among infants requiring multidrug therapy for symptom control, there was a lower mean fat percent and fat-free mass compared to infants requiring monotherapy. Infants with neonatal abstinence syndrome were smaller and leaner during early life compared to term infants. The authors conclude that infants with more severe neonatal abstinence syndrome (requiring multidrug therapy) may be at risk of abnormalities in long-term growth.

Cardiac and vascular health in late preterm infants. Dissanayake and colleagues assessed 35 healthy late preterm newborn infants with normal growth compared to term born infants for aortic anatomy and cardiac autonomic control. Infants born late preterm demonstrated several differences in markers of cardiovascular risk, with beneficial differences in aortic wall thickness and potentially detrimental differences in autonomic control. The authors suggest that these findings provide evidence to support the increased risk of hypertension and sudden cardiac death in individuals born late preterm.

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