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In This Issue

This first Issue of *Journal of Developmental Origins of Health and Disease* contains two outstanding Reviews on the concepts and economic impact of programming of adult disease, and a series of Original Articles spanning human epidemiologic studies to investigations of mechanistic hypotheses in animal models ranging from small to large species. The Commentary on the Original Article by Mazumder *et al*. is a highly pertinent assessment of the effects of the 1918 influenza pandemic, in view of our current H1N1 epidemic.

Human studies of DOHaD mechanisms

A conceptual framework for DOHaD: In the first paper, Gluckman, Hanson and Buklijas provide a historical review of the research linking development and adult diseases and assess the evolutionary and developmental significance of DOHaD. The authors discuss how modern medicine has primarily focused on disease-specific organ pathology. DOHaD now has extended the potential for medicine to focus on the perinatal environment as an etiology for adult diseases.

The economic cost of a poor start to life: In the second Review of this Issue, Alderman assesses the economic consequences of malnutrition. Whereas infant mortality has been a traditional measured outcome of low birth weight, Alderman demonstrates how long-term consequences including adult physical productivity, cognitive ability, chronic diseases and even inter-generational benefits, far exceed the traditional costs. The economic implications of DOHaD provide a compelling argument for public policy approaches.

Prenatal effects of the 1918 influenza pandemic on adult cardiovascular disease: In the first Original Article, Mazumder *et al*. utilize a unique data base of adults born in the 1918–1919 birth cohorts, demonstrating a greater than 20% excess cardiovascular disease at age 60–82 years. The authors suggest that *in utero* inflammation resulting from maternal influenza and secondary infection promotes later vascular aging and metabolic disorders.

Maternal predictors of neonatal bone development: Harvey *et al*. utilize the Southampton Women's Survey to evaluate the relationship between maternal life style and body composition with neonatal bone size and structure. Increased maternal parity and fat stores were associated with greater neonatal bone area and bone mineral content, while maternal smoking was associated with lower neonatal bone mass. The Southampton Women's Survey cohort of over 12,000 women will continue to provide quality information regarding maternal predictors of DOHaD.

Animal studies of DOHaD mechanisms

Foetal hypoglycaemia and cardiovascular studies: In the first of the animal studies, Cleal *et al*. examine the effect of late gestation fetal hypoglycemia on cardiovascular and endocrine function in sheep. With the escalating rate of maternal diabetes, human fetuses are often exposed to both hypo and hyperglycemic conditions. Cleal *et al*. induced ovine fetal hypoglycemia via an intravenous insulin infusion to the ewe. Maternal and fetal hypoglycemia was associated with a decreased fetal heart rate, and increased blood pressure responses to umbilical cord occlusion and reduced fetal baroreflex sensitivity. These responses may have important implications for the risk of cardiovascular disease in later life.

Postnatal growth and metabolic function: van der Linden et al complement the study of Cleal *et al*., in demonstrating the long-term impact of female lambs born to dams which received altered nutritional regimens. The results suggest that offspring born to heavy dams had greater postnatal growth rates after puberty and an increased predisposition to glucose intolerance and insulin resistance in adult life.

Altitude-induced fetal cardiovascular remodeling: Salinas *et al*. utilized the chick embryo model to demonstrate that hypoxia triggers slow fetal growth and aortic thickening. Of note, parallel human clinical studies have reported that babies born from pregnancies complicated by placental insufficiency show aortic thickening with increased vascular stiffness and reduced distensibility. These studies in the chick embryo indicate that prenatal hypoxia, whether due to placental insufficiency or high altitude, is a likely stimulus for the developmental programming of adult diseases.

Programmed fetal nephrogenesis: Henry *et al*. utilized an undernourished rat model to examine programming mechanisms of reduced nephrogenesis. The authors confirmed that GDNF and MAPK-ERK signal pathways are dysregulated during active nephrogenesis in fetal and early newborn kidneys, and may represent a key mechanism in both reduced offspring nephrogenesis and programmed hypertension.

Proteinuria in aging rats: In a complementary study of programmed nephrogenesis, Joles *et al*. demonstrated that maternal low protein intake during early nephrogenesis may induce long-term renal injury in rats. Adult rats exposed to a low protein maternal environment demonstrated significantly increased proteinurea, indicative of renal injury. The loss of renal function was greater in male rats and was associated with a disturbance of antioxidant status and increased apoptosis.

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