

Abstracts

Obesity, male infertility, and the sperm epigenome

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Obesity is a growing epidemic and a common problem among reproductive-age men that can both cause and exacerbate male-factor infertility by means of endocrine abnormalities, associated comorbidities, and direct effects on the fidelity and throughput of spermatogenesis. Robust epidemiologic, clinical, genetic, epigenetic, and nonhuman animal data support these findings. Recent works in the burgeoning field of epigenetics has demonstrated that paternal obesity can affect offspring metabolic and reproductive phenotypes by means of epigenetic reprogramming of spermatogonial stem cells. Understanding the impact of this reprogramming is critical to a comprehensive view of the impact of obesity on subsequent generations. Furthermore, and perhaps more importantly, conveying the impact of these lifestyle changes on future progeny can serve as a powerful tool for obese men to modify their behavior. Reproductive urologists and endocrinologists must learn to assimilate these new findings to better counsel men about the importance of paternal preconception health, a topic recently being championed by the Centers for Disease Control and Prevention.

Obesity and female infertility: potential mediators of obesity's impact

Darcy E. Broughton, M.D., Kelle H. Moley. *Fertil Steril.* 2017. 107(4):840–847

The worldwide upward trend in obesity has been dramatic, now affecting more than 20% of American women of reproductive age. Obesity is associated with many adverse maternal and fetal effects prenatally, but it also exerts a negative influence on female fertility. Obese women are more likely to have ovulatory dysfunction due to dysregulation of the hypothalamic-pituitary-ovarian axis. Women with polycystic ovarian syndrome who are also obese demonstrate a more severe metabolic and

reproductive phenotype. Obese women have reduced fecundity even when eumenorrheic and demonstrate poorer outcomes with the use of in vitro fertilization. Obesity appears to affect the oocyte and the preimplantation embryo, with disrupted meiotic spindle formation and mitochondrial dynamics. Excess free fatty acids may have a toxic effect in reproductive tissues, leading to cellular damage and a chronic low-grade inflammatory state. Altered levels of adipokines, such as leptin, in the obese state can affect steroidogenesis and directly affect the developing embryo. The endometrium is also susceptible, with evidence of impaired stromal decidualization in obese women. This may explain subfecundity due to impaired receptivity, and may lead to placental abnormalities as manifested by higher rates of miscarriage, stillbirth, and preeclampsia in the obese population. Many interventions have been explored to mitigate the effect of obesity on infertility, including weight loss, physical activity, dietary factors, and bariatric surgery. These data are largely mixed, with few high quality studies to guide us. As we improve our understanding of the pathophysiology of obesity in human reproduction we hope to identify novel treatment strategies.

Timing of antenatal corticosteroid administration and survival in extremely preterm infants: a national population-based cohort study

H Norberg, J Kowalski, K Maršál, M Norman. *BJOG.* 2017;124(10):1567–1574.

Objective: To explore the association between administration-to-birth interval of antenatal corticosteroids (ACS) and survival in extremely preterm infants.

Design: Population-based prospective cohort study.

Setting: All obstetric and neonatal units in Sweden from 1 April 2004 to 31 March 2007.

Population: All live-born infants (n = 707) born at 22–26 completed weeks of gestation.

Methods: The relationship between time from first administration of ACS to delivery and survival was investigated using Cox proportional hazards regression analysis.

Main outcome measures: Neonatal (0–27 days) and infant (0–365 days) survival, and infant survival without major neonatal morbidity (intraventricular haemorrhage grade e" 3, retinopathy of prematurity stage e" 3, periventricular leukomalacia, necrotising enterocolitis, or severe bronchopulmonary dysplasia).

Results: Five-hundred and ninety-one (84%) infants were exposed to ACS. In the final adjusted model, infant survival was lower in infants unexposed to ACS [hazard ratio (HR) = 0.26; 95% confidence interval 0.15–0.43], in infants born <24 h [HR = 0.53 (0.33–0.87)] and >7 days after ACS [HR = 0.56 (0.32–0.97)], but not in infants born 24–47 h after ACS [HR

= 1.60 (0.73–3.50)], as compared with infants born 48 h to 7 days after administration. The findings were similar for neonatal survival. Survival without major neonatal morbidity among live-born infants was 14% in unexposed infants and 30–39% in steroid-exposed groups, indicating that any ACS exposure was valuable.

Conclusions: Administration of ACS 24 h to 7 days before extremely preterm birth was associated with significantly higher survival than in unexposed infants and in infants exposed to ACS at shorter or longer administration-to-birth intervals.