Dad's exposure to phthalates in plastics may affect embryonic development

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A new study led by environmental health scientist Richard Pilsner at the University of Massachusetts Amherst, one of the first to investigate whether preconception exposures to phthalates in fathers has an effect on reproductive success via embryo quality, found that exposures from select chemicals tested were associated with "a pronounced decrease in blastocyst quality" at an early stage in embryo development.

Phthalates are compounds found in plastics and personal care products that are estimated to be detectable in nearly 100 percent of the U.S. population. The authors believe theirs is the first prospective study to assess associations between paternal exposure to phthalates and embryo quality through the blastocyst stage in humans.

Pilsner and colleagues say their prospective study of 761 oocytes, or immature eggs, from 50 couples undergoing in vitro fertilization (IVF) "provides the first data demonstrating associations between preconception paternal phthalate and phthalate alternatives and embryo development, in a critical step towards our understanding of the paternal contributions to reproductive success." Details appear in the current issue of *Human Reproduction* from Oxford University Press.

For this investigation, the researchers recruited 50 couples from the Baystate Medical Center's Fertility Center in Springfield, Mass., as part of the Sperm Environmental Epigenetics and Development Study (SEEDS). They measured phthalate exposure in urine from male and female partners on the same day as semen sample procurement and oocyte retrieval, and assessed embryo quality at the cleavage (day 3) and blastocyst (day 5) stages.

The 50 couples contributed 761 oocytes, of which 423 progressed to the cleavage stage, 261 were high quality cleavage stage embryos, 137 were transferrable quality blastocysts and 47 were high quality blastocysts.

The researchers quantified concentrations of 17 urinary metabolites by liquid chromatography mass spectrometry, estimated odds ratios (OR) and confidence intervals with urinary phthalates and phthalate alternatives fitted as continuous variables and embryo quality as a binary variable.

At the cleavage stage, there were no overall significant associations for

male or female phthalate exposures. Concentrations of male urinary monoethyl phthalate were positively associated with high quality cleavage stage embryos, with an OR=1.20 and no other significant associations were observed at this stage. At the blastocyst stage, ORs for male urinary concentrations of monobenzyl phthalate was 0.55 for mono-3-hydroxybutyl phthalate 0.37, for mono-n-butyl phthalate 0.55 and for monomethyl phthalate 0.39, all inversely associated with high-quality blastocysts.

"Although our results do not show altered embryo development associated with urinary metabolites at day 3, it is possible that the molecular changes associated with phthalates and phthalate alternatives were too subtle to be detected morphologically during these early cleavage stages and that such early molecular changes manifest at the morphological level during later stages of development," the authors say.

"Our modest sample included only 50 couples contributing one cycle each. In addition, non-differential misclassification of exposure remains a concern given the single spot urine collection and the short half-life of phthalates," they add. Overall, results support "the growing evidence that the preconception paternal environmental health may contribute to reproductive potential."

They add that "future studies are needed to investigate the long-term effects of altered embryo development" and to identify a mechanism by which a father's preconception exposure to phthalates may affect embryo development. "If corroborated with other studies, such findings will have public health and clinical significance for both the general population and those undergoing IVF."

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