**MATERNAL EXPOSURE TO DI(2-ETHYHEXYL)PHTHALATE IMPACTS FETAL CARDIAC DEVELOPMENT**

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*Objective*: This study aims to explore the associations between maternal occupational exposures to phthalates (a commonly used phthalate ester plasticizer,) periconceptionally and isolated congenital heart defects (CHDs) in human, and to evaluate the effects of maternal DEHP exposures on fetal cardiac development in mice.

*Methods*: A case control study with standardized data collection involving 761 children with isolated CHDs and 609 children without any congenital malformations was conducted. An adjusted job exposure matrix was used for maternal occupational DEHP exposure assessment. Logistic regression analysis was performed to assess the associations between maternal occupational DEHP exposures and CHDs. Totally, 75 female pregnant C57BL mice were randomized equally into 5 groups consisting the blank group, vehicle group, and three DEHP groups (0.5g/Kg, 1g/Kg and 2g/Kg). Pregnant dams in different groups received respective intervention by gavage once daily from E6.5-E14.5. HE staining was used to examine the fetal cardiac malformations. Fetal cardiac development-related genes (Nkx2.5, GATA4, TBX5, MEF2C, CHF1) mRNA and protein expression were determined by real-time quantitative PCR and WB.

*Results*: Maternal occupational exposures to phthalates periconceptionally are associated with perimembranous ventricular septal defect (PmVSD) (P=0.001, adjusted OR 3.7, 95%CI 1.7¨C8.0), patent ductus arteriosus (PDA) (P=0.002, adjusted OR 3.8, 95%CI 1.6¨C8.9), secundum atrial septal defect (s-ASD) (P=0.008, adjusted OR 3.5, 95%CI 1.4¨C8.7) and pulmonary valve stenosis (PS) (P= 0.035, adjusted OR 4.2, 95%CI 1.1¨C16.0). Maternal exposures to DEHP could induce various fetal cardiac malformations (including septal defects, myocardial developmental abnormalities, hypoplasia) in mice with a dose-dependent matter. The GATA4, MEF2C and CHF1 mRNA and protein expression of fetal heart were significantly down-regulated by DEHP.

*Conclusions:* Maternal exposures to phthalates periconceptionally increase the risk of some CHDs phenotype. Administration of DEHP can result in various fetal cardiac malformations in mice.