

URINARY MARKERS OF FETAL EXPOSURES TO PHTHALATES AND PHENOLS AND RISK OF MALE GENITAL ANOMALIES, IN EDEN AND PELAGIE MOTHER-CHILD COHORTS

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Background and Aims: Exposure during pregnancy to chemicals suspected to disrupt hormonal signalling may alter male reproductive organogenesis, which is controlled by sex hormones. Our aim was to assess the association between risk of hypospadias and undescended testis at birth and fetal exposure to phthalates and phenols.

Methods: We conducted a case-control study nested in two French mother-child cohorts (EDEN, PELAGIE) that enrolled pregnant women between 2002 and 2006. Cases were all boys members of the cohorts with hypospadias (n=21) or undescended testis (n=50) at birth. Three matched controls per case were selected among male singleton livebirths. Eleven phthalate metabolites and 9 phenols (EDEN cohort only) concentrations were measured in the pregnant mothers' urine collected between the 3rd and the 28th gestational week. Conditional logistic analyses adjusted for maternal age, parity, educational level, gestational duration and urinary creatinine were carried out.

Results: Prevalence ranged from 0.3% to 1.1% for hypospadias and from 0.7% to 5.1% for undescended testis according to residence area. Decreased risk of hypospadias, but not statistically significant, was observed with urinary concentrations of both low- and high-molecular-weight phthalate metabolites (p_trend, 0.13 and 0.10, respectively). No evidence of association (p_trend>0.10) with urinary concentrations of phthalates metabolites was observed for undescended testis risk. Risk of undescended testis increased with urinary concentrations of ethylparaben (OR_1st_tertile=reference; OR_2nd_tertile=1.5, 0.4-5.3; OR_3rd_tertile=2.9, 0.9-9.9; p_trend=0.08). Excluding preterm births led to similar conclusions.

Conclusions: Our study did not support an impact of fetal exposure to phthalates or bisphenol A on male genital tract development. It however pointed out a possible role of ethylparaben on testicular descent which needs to be replicated by further studies since it is not supported by animal data. Our study was limited by a modest sample size but provided prenatal exposure assessment (that covers the gestational window of male reproductive organogenesis).