Amniotic fluid phthalate levels and male fetal gonad function.

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Source: Epidemiology. 2015 Jan;26(1):91-9
Date: Jan-2015
Language: English
Publication Type: Article

Keywords: Adult
Amniotic Fluid - chemistry
Case-Control Studies
Cryptorchidism - epidemiology
Denmark - epidemiology
Diethylhexyl Phthalate - analysis
Environmental Exposure - statistics & numerical data
Female
Gonadal Steroid Hormones - analysis
Humans
Hydrocortisone - analysis
Hypospadias - epidemiology
Immunoassay
Infant, Newborn
Insulin - analysis
Leydig Cells
Linear Models
Logistic Models
Male
Mass Spectrometry
Phthalic Acids - analysis
Pregnancy
Proteins - analysis

Abstract: Prenatal exposure to phthalates may pose a threat to human male reproduction. However, additional knowledge about the in vivo effect in humans is needed, and reported associations with genital abnormalities are inconclusive. We aimed to study prenatal di(2-ethylhexyl) phthalate (DEHP) and diisononyl phthalate (DiNP) exposure in relation to cryptorchidism, hypospadias, and human fetal Leydig cell function.

We studied 270 cryptorchidism cases, 75 hypospadias cases, and 300 controls. Second-trimester amniotic fluid samples were available from a Danish pregnancy-screening biobank (n = 25,105) covering 1980-1996. We assayed metabolites of DEHP and DiNP (n = 645) and steroid hormones (n = 545) by mass spectrometry. We assayed insulin-like factor 3 by immunoassay (n = 475) and analyzed data using linear or logistic regression.

Mono(2-ethyl-5-carboxypentyl) phthalate (5cx-MEPP, DEHP metabolite) was not consistently associated with cryptorchidism or hypospadias. However, we observed an 18% higher (95% confidence interval [CI] = 5%-33%) testosterone level, and a 41% lower (-56% to -21%) insulin-like factor 3 level in the highest 5cx-MEPP tertile compared with the lowest. Mono(4-methyl-7-carboxyheptyl) phthalate (7cx-MMeHP, DiNP metabolite) showed elevated odds ratio point estimates for having cryptorchidism (odds ratio = 1.28 [95% CI = 0.80 to 2.01]) and hypospadias (1.69 [0.78 to 3.67]), but was not consistently associated with the steroid hormones or insulin-like factor 3.

Data on the DEHP metabolite indicate possible interference with human male fetal gonadal function. Considering the DiNP metabolite, we cannot exclude (nor statistically confirm) an association with hypospadias and, less strongly, with cryptorchidism.

PubMed ID: 25384265 View in PubMed

Phthalates and perfluorooctanesulfonic acid in human amniotic fluid: temporal trends and timing of amniocentesis in pregnancy.

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Source: Environ Health Perspect. 2012 Jun;120(6):897-903
Date: Jun-2012
Language: English
Publication Type: Article
Keywords: Alkanesulfonic Acids - analysis
Amniocentesis - methods
Amniotic Fluid - chemistry
Chromatography, Liquid
Denmark
Environmental Pollutants - analysis
Female
Fluorocarbons - analysis
Gestational Age
Humans
Linear Models
Male
Mass Spectrometry
Maternal Exposure - statistics & numerical data
Phthalic Acids - analysis
Pregnancy

Abstract: Measures of prenatal environmental exposures are important, and amniotic fluid levels may directly reflect fetal exposures during hypothesized windows of vulnerability.

We aimed to detect various phthalate metabolites and perfluorooctanesulfonic acid (PFOS) in human amniotic fluid, to study temporal exposure trends, and to estimate potential associations with gestational week of amniocentesis and maternal age and parity at amniocentesis.

We studied 300 randomly selected second-trimester amniotic fluid samples from a Danish pregnancy-screening biobank covering 1980 through 1996. We used only samples from male offspring pregnancies. We assayed the environmental pollutants by liquid chromatography/triple quadrupole mass spectrometry and analyzed data using generalized linear regression models.

We detected the di(2-ethylhexyl) phthalate (DEHP) metabolite mono(2-ethyl-5-carboxypentyl) phthalate (5cx-MEPP) at a median concentration of 0.27 ng/mL [interquartile range (IQR): 0.20-0.37 ng/mL], the diisononyl phthalate (DiNP) metabolite mono(4-methyl-7-carboxyheptyl) phthalate (7cx-MMeHP) at 0.07 ng/mL (IQR: 0.05-0.11 ng/mL), and PFOS at 1.1 ng/mL (IQR: 0.66-1.60 ng/mL). An increase of 1 calendar year was associated with 3.5% lower [95% confidence interval (CI): -4.8%, -2.1%] 5cx-MEPP levels and with 7.1% higher (95% CI: 5.3%, 9.0%) 7cx-MMeHP levels. For each later gestational week of amniocentesis, 5cx-MEPP was 9.9% higher (95% CI: 4.8%, 15.2%), 7cx-MMeHP was 8.6% higher (95: CI: 2.7%, 14.9%), and PFOS was 9.4% higher (95: CI: 3.3%, 15.9%). We observed no associations with maternal age or parity.

Measured metabolite levels appeared to parallel decreasing DEHP exposure and increasing DiNP exposure during the study period. The environmental pollutant levels were positively associated with later gestational age at amniocentesis during pregnancy weeks 12-22.

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PubMed ID: 22398305 View in PubMed