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Prenatal paraben endocrine disruptor exposure and the association with sex steroid hormone levels: A 11-year follow-up birth cohort study

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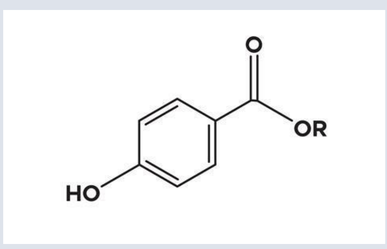
BACKGROUND AND OBJECTIVE

Paraben (an antimicrobial preservative para-hydroxybenzoic acid) (**Fig. 1**) is commonly used in foods, drugs and cosmetics and have been well established as environmental endocrine disruptors. However, few studies have examined their effects on sex steroid hormones in children. Recently, fetal origin of health and disease in adults has been of concerns. We followed children over time to examine the association between prenatal paraben exposure and sex steroid hormone levels at 2, 5, 8, and 11 years of age.



MP, R = $-CH_3$ PP, R = $-CH_2CH_2CH_3$
EP, R = $-CH_2CH_3$ BP, R = $-CH_2CH_2CH_2CH_3$

Figure 1. Structure of paraben

MATERIALS AND METHODS

- Subjects
  We recruited 430 pregnant women from central Taiwan from 2000 to 2001 and followed up their children at birth, 2, 5, 8, and 11 years of age. A total of 364 newborns whose mothers had provided a maternal urine sample in the 3rd trimester were recruited in the follow-up study (**Fig. 2**).
- Measurements
  Testosterone (TT) (ng/mL), free testosterone (free TT) (pg/mL), and Estradiol (E_2) (pg/mL) were measured from venous blood. Four parabens (μg/L), including methyl paraben (MP), ethyl paraben (EP), propyl paraben (PP), and butyl paraben (BP) (**Fig. 1**), were measured in maternal urine collected during the 3rd trimester by Liquid Chromatograph Tandem Mass Spectrometer.
- Statistical analysis
  Generalized estimating equation (GEE) regression analysis with repeated measures was used to estimate associations between paraben and hormone levels.

RESULTS

A total of 164 children who had at least one follow-up at 2, 5, 8, and 11 years, and had measurements for both paraben and hormone levels were included (**Fig. 2**). We further excluded girls (n = 10) who had menarche at the age of 11 years. The characteristics of included children and their mothers are reported in **Fig. 3**.

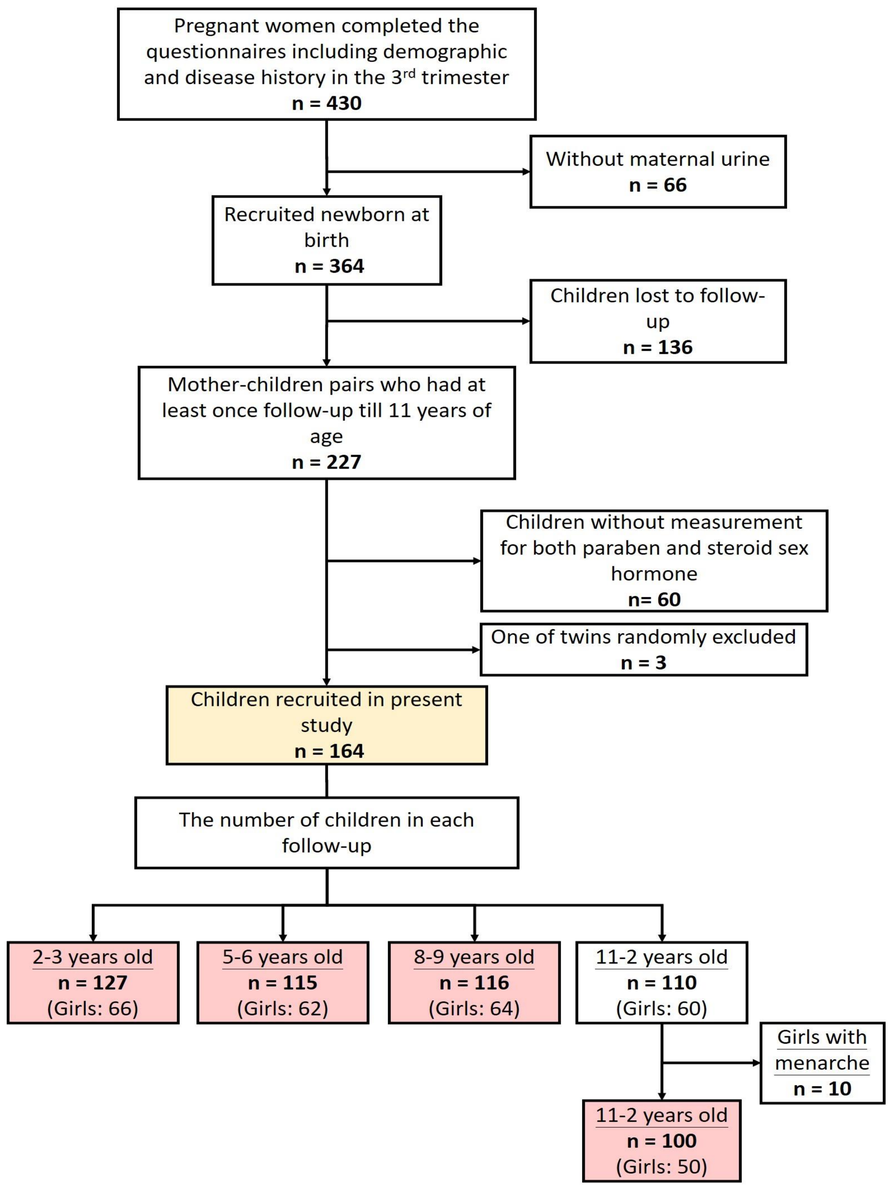


Figure 2. Flow chart of participant recruitment

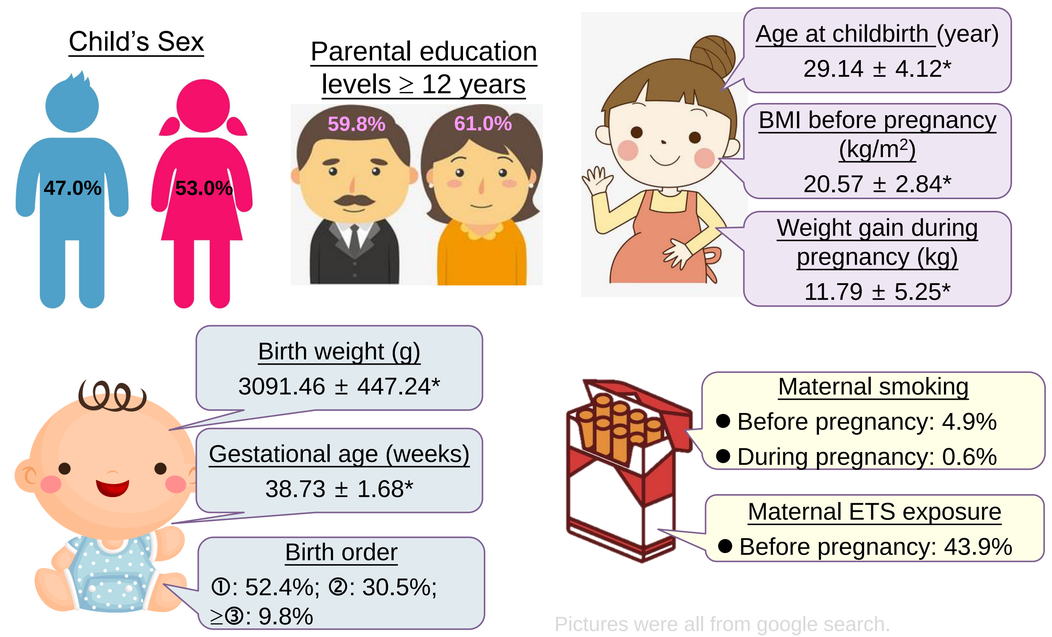


Figure 3. Characteristics of recruited participants (n = 164).

***mean ± SD.**

Fig 4. demonstrated Spearmen's correlation between maternal paraben concentrations and sex hormone levels. In boys, a negative correlation was found between maternal MP and TT at aged 11 years (-0.0325, p = 0.025) and maternal BP and TT at age 8 years (-0.309, p = 0.031).

The beta statistics from the GEE analyses for sex steroid hormone levels in relation to maternal urinary paraben levels were reported in **Fig. 5** After adjustment for potential confounders, maternal MP was associated with increased levels of E2 in boys (β = 0.038, p = 0.042).

CONCLUSION

Prenatal paraben exposure may alter sex steroid hormones of children over time, which may pose potential reproductive health risks.

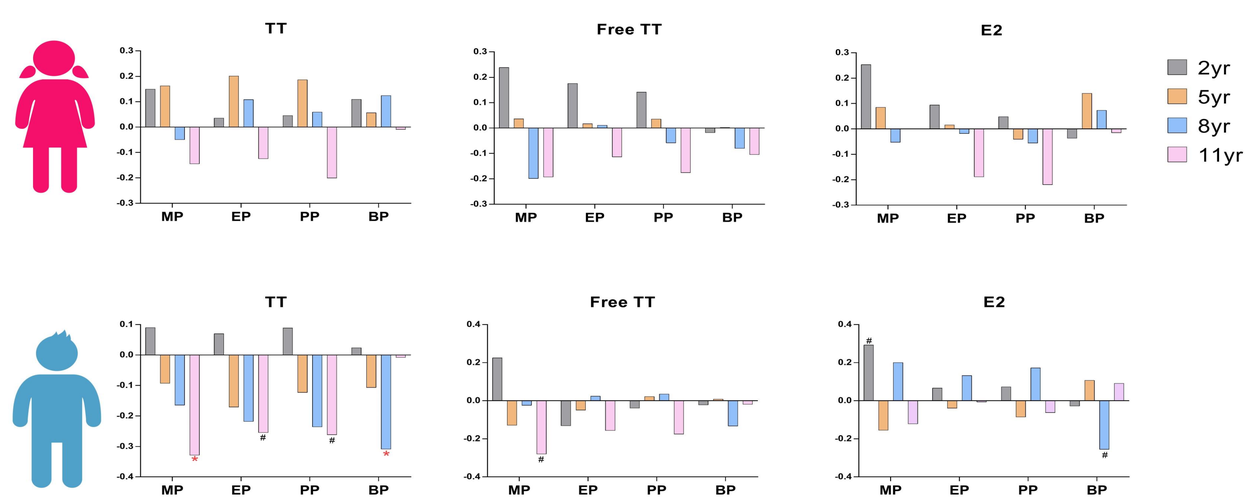


Figure 4. Spearman's correlation between maternal paraben concentrations and sex steroid hormone levels in children by follow-up age (n = 164).

#p<0.1; *p<0.05.

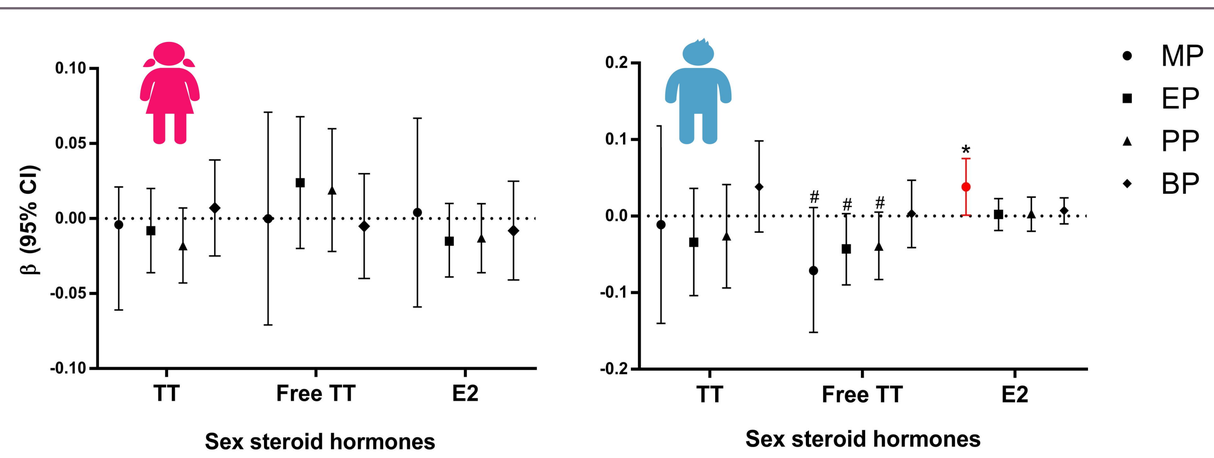


Figure 5. Betas from the generalized equation estimate (GEE) linear regression for sex steroid hormone levels in relation to maternal urinary paraben levels (μg/g creatinine) (n = 164).

#p<0.1; *p<0.05.

GEE model was adjusted for child's age and BMI at time of follow-up, and maternal age at childbirth, BMI before pregnancy, smoking and drinking habits during pregnancy.

- The study process was approved by the Research Ethics Committee of the National Health Research Institutes and Chung Shan Medical University Hospital in Taiwan.
- All authors have no financial conflicts of interests to declare.