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# **Endocrine Disruptors in the Workplace, Hair Spray, Folate Supplementation, and Risk of Hypospadias: Case-control Study**

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**Running title:** Endocrine Disruptors, Hair spray, Folate and Hypospadias

**Key words:** endocrine disruptors, hair spray, folate supplementation, hypospadias, occupation

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### **Abbreviations:**

DBP dibutyl phthalate

DEP diethyl phthalate;

EDCs endocrine disrupting chemicals

MBP mono-n-butyl phthalate

MEP monoethyl phthalate

ONS Office for National Statistics.

## **Outline of section headings**

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## **ABSTRACT**

**BACKGROUND:** Hypospadias is one of the commonest urogenital congenital anomalies affecting baby boys. Prevalence estimates in Europe range from 4 to 24 per 10,000 births, depending on definition with higher rates reported from the United States. Relatively little is known about potential risk factors, but a role for endocrine disrupting chemicals has been proposed.

**OBJECTIVE:** To elucidate risk of hypospadias associated with occupational exposure of the mother to endocrine disruptor chemicals, use of folate supplementation during pregnancy, and vegetarianism.

**DESIGN:** Case-control study of 471 hypospadias cases referred to surgeons, and 490 randomly selected birth controls, born 1 January 1997 to 30 September 1998, south-east England. Telephone interview of mothers, including information on folate supplementation during pregnancy and vegetarianism, and a job exposure matrix to classify occupational exposure.

**RESULTS:** In multiple logistic regression analysis, there were increased risks for self-reported occupational exposure to hairspray (exposed vs non exposed OR 2.39 95% CI 1.40, 4.17), and phthalate exposure obtained by a job exposure matrix (OR 3.12 95% CI 1.04, 11.46). There was a significant protective effect of folate use during the first three months of pregnancy (OR 0.64 95% CI 0.44, 0.93). Vegetarianism was not associated with hypospadias risk.

**CONCLUSIONS:** Excess risks of hypospadias associated with occupational exposures to phthalates and hair spray suggest that anti-androgenic endocrine disrupting chemicals may play a role in hypospadias. Folate supplementation in early pregnancy may be protective.