

## Exposure to chemicals in plastic and fungicides may irreversibly weaken children's teeth

Chemicals commonly found in plastics and fungicides may be weakening children's teeth by disrupting hormones that stimulate the growth of dental enamel, according to a new study presented today at the European Congress of Endocrinology.

Endocrine disruptors are chemicals that interfere with mammalian hormones. Bisphenol A (BPA) is one of the most prevalent, found in every-day items including refillable drink bottles and food storage containers. Vinclozolin is another endocrine disruptor that was commonly used as a fungicide in vineyards, golf courses and orchards.

Molar incisor hypermineralisation (MIH) is a pathology affecting up to 18% of children aged 6-9, in which the permanent first molars and incisors teeth that erupt have sensitive spots that become painful and are prone to cavities. These spots are found on dental enamel, the tough outer covering of teeth that protects it from physical and chemical damage. Unlike bone, enamel does not regrow and so any damage is irreversible. Previous rat studies have shown that MIH may result from exposure to BPA after finding similar damage to the enamel of rats that received a daily dose of BPA equivalent to normal human BPA exposure, though the exact mechanism of action remains unclear.

In this study, researchers from the French National Institute of Health and Medical Research (INSERM) gave rats daily doses of BPA alone or in combination with vinclozolin, equivalent to an average dose a human would experience daily, from birth till they were thirty days old. They then collected cells from the rats' teeth surface and found that BPA and vinclozolin changed the expression of two genes controlling the mineralisation of tooth enamel.

In part two of their experiment, the team cultured and studied rat ameloblast cells, which deposit enamel during the development of teeth. They found that the presence of sex hormones like oestrogen and testosterone boosted the expression of genes making tooth enamel, especially male sex hormones. As BPA and vinclozolin are known to block the effect of male sex hormones, the findings reveal a potential mechanism by which endocrine disruptors are weakening teeth.

"Tooth enamel starts at the third trimester of pregnancy and ends at the age of 5, so minimising exposure to endocrine disruptors at this stage in life as a precautionary measure would be one way of reducing the risk of enamel weakening", said Dr Katia Jedeon, lead author of the study.

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## Abstract

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### **Systemic enamel pathologies may be due to anti-androgenic effects of some endocrine disruptors**

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There has been increasing concerns over the last twenty years about the potential adverse effects of endocrine disruptors (EDs). Anecdotally, molar incisor hypomineralization (MIH), a recently described enamel pathology, now affecting 15 to 18% of 6-9 years old children, is increasing concurrently with ED related pathologies. Our previous data show that bisphenol A (BPA) and vinclozolin, two anti-androgenic EDs, impact amelogenesis and enamel mineralization preferentially in male rats and generate similar enamel defects as those described for MIH. The resulting irreversible enamel defects may provide an easily accessible marker for reporting early ED exposure in humans. The aim of the present study was to decipher the mechanism of action of low-dose ED during amelogenesis. Wistar rats were exposed to low-dose EDs from the first day of gestation to 30 days after birth. Global transcriptomic analysis showed BPA and vinclozolin modulated the expression of a small group of genes directly involved in enamel mineralization, among them the protease KLK4 and the ion-exchanger SLC5A8 which are crucial for amelogenesis. Analysis of the ED putative receptor expression pattern showed that in contrary to estrogen receptor  $\alpha$  (ER $\alpha$ ) which is mainly expressed by ameloblastic precursors, androgen receptor (AR) was 3- to 5-fold more expressed in full differentiated ameloblasts responsible of enamel mineralization. In vivo and in vitro analysis carried out on the rat ameloblastic cell line HAT-7 and human androgen-sensitive prostate cancer cells LNCaP showed AR nuclear translocation upon testosterone treatment, and testosterone up-regulation of two enamel specific gene expression (KLK4 and SLC5A8). This induction occurred at the transcriptional level and was inhibited by siRNAs directed against AR as well as by vinclozolin and BPA. In conclusion, we report that 1) dental epithelial cells are sensitive to estrogens and androgens, 2) amelogenesis is modulated by androgens and that 3) two anti-androgenic EDs, BPA and vinclozolin, irreversibly disrupt this process preferentially in male rats by modulating the transcription of enamel specific genes. We thus provide evidence of hormonal influence on amelogenesis and probably on sexual differences of enamel quality.

## Notes for Editors

1. For further information about the study please contact:

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2. The study "[Systemic enamel pathologies may be due to anti-androgenic effects of some endocrine disruptors](#)" will be presented at 11.45AM on Tuesday 31 May 2016 at the European Congress of Endocrinology at the ICM in Munich, Germany.
3. For other press enquiries please contact the ECE 2016 press office:

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4. The European Congress of Endocrinology is held at the Internationales Congress Center München between 28-31 May 2016.
5. The [European Society of Endocrinology](#) was created to promote research, education and clinical practice in endocrinology by the organisation of conferences, training courses and publications, by raising public awareness, liaison with national and international legislators, and by any other appropriate means.