# APPENDIX- RECENT UPDATES ON ENDOCRINE DISRUPTING CHEMICALS (EDCs)

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## PRENATAL EXPOSURE AND FETAL DEVELOPMENT

Recent studies have shown that prenatal exposure to endocrine disrupting chemicals (EDCs) can significantly impact fetal development. The HPP-3D (Human Placental Plasticity–3D) study found a negative association between maternal phthalate levels and fetal liver volume, with changes comparable to a 5 kg/m² difference in parental Body Mass Index suggesting early structural alterations with potential lifelong metabolic consequences (1). In the Ko-CHENS (Korean Children’s Environmental Health Study ) study, personal care product use was linked to higher levels of monoethyl phthalate (MEP), and cooking with plastic was associated with increased mono-n-butyl phthalate (MNBP) levels (2). The Let's R.O.A.R (Let’s Reclaim Our Ancestral Roots) pilot intervention demonstrated that culturally tailored strategies could reduce low-molecular weight phthalate metabolites by over 5% in Black women, particularly dibutyl phthalate (3).

## Neurodevelopment and Behavioral Outcomes

EDCs have also been implicated in neurodevelopmental and behavioral disorders. The PELAGIE (Perturbateurs Endocriniens: Étude Longitudinale sur les Anomalies de Grossesse, l’Infertilité et l’Enfance) cohort from France found that exposure to perfluorinated compounds such as perfluorooctanoic acid (PFOA), (perfluorononanoic acid) PFNA, and perfluorodecanoic acid (PFDA) was associated with externalizing and internalizing behaviors in children (4). Bisphenol A (BPA) was found to be associated with aromatase gene methylation and autism spectrum disorder (ASD) traits in boys, with reversibility shown in mouse models using !0-hydroxy-2-decenoic acid(10HDA), suggesting a potential therapeutic pathway (5). Another study identified BPA interaction with 35 of 77 ASD-related genes in transcriptomic analysis (6). A systematic review concluded that EDC exposure, especially to metals, phthalates, and PFAS is linked to poorer cognitive, language, and motor development in children, with girls being more susceptible (7).

**FEMALE REPRODUCTIVE HEALTH AND OVARIAN FUNCTION**

The Study of Women’s Health Across the Nation (SWAN) found that exposure to heavy metals like arsenic, cadmium, and mercury was associated with lower anti-Müllerian hormone (AMH) levels and a faster premenopausal decline (8). A human ovarian model exposed to diethylstilbestrol (DES) and ketoconazole (KTZ) showed altered follicle survival and steroidogenesis, with upregulation of stearoyl-CoA desaturase (SCD) and 7-dehydrocholesterol reductase, indicating potential biomarkers for ovarian toxicity (9). Microplastics (MPs) have been detected for the first time in human ovarian follicular fluid, in 14 out of 18 women undergoing IVF, with an average of 2,191 particles/mL. A significant correlation has been observed between MP levels and FSH, suggesting potential effects on ovarian function. While no link has been found with fertilization or pregnancy outcomes, the findings highlight a concerning new avenue for understanding the reproductive impact of microplastic exposure (10). In a rat model, di(2-ethylhexyl) phthalate (DEHP) exposure induced polycystic ovary syndrome (PCOS)-like changes, insulin resistance, and oxidative stress via the PPARγ pathway (11).

## COGNITIVE AGING

EDC exposure may also affect cognitive aging. Analysis of NHANES data (2011–2014) linked exposure to 47 EDCs, including PFNA, PCB-199, and PCB-206, with worse verbal fluency and global cognition, though delayed recall effects were mixed (12).

## PUBERTY AND HORMONAL PATHWAYS

In vitro analysis using the Tox21 10K library identified musk ambrette and methacholine analogs as agonists of KISS1R and GnRHR, suggesting that they may promote early puberty through hormonal activation (13).

## TOXICOLOGY AND RISK ASSESSMENT

Regulatory and technological advancements in EDC detection and safety evaluation are ongoing. The European Food Safety Authority (EFSA) revised the tolerable daily intake for BPA from 4 µg/kg/day to 0.2 ng/kg/day, indicating increased concern over low-dose effects (14). New Approach Methods (NAMs), including in vitro and in silico tools, were used to prioritize over 200 low-data chemicals for further study (15). An electrochemical sensor using a 2D-Al quasicrystal structure detected PFOA with high sensitivity (16). Concerns have been raised regarding the toxicity and potential endocrine disrupting effects of UV filters used in sunscreens. Six commonly used organic UV filters were assessed using the ToxCast/Tox21 database and found that they exhibited low biological activity, with most effects occurring at concentrations above cytotoxic levels. Except for oxybenzone, human plasma levels were significantly lower than those causing activity in assays. Overall, these UV filters showed weak or negligible endocrine-disrupting potential, supporting their low risk to human health(17).

**CONCLUSION**

The growing body of evidence highlights the pervasive impact of EDCs on female reproductive and metabolic health across the life course. From fetal development to menopause, EDCs such as phthalates, bisphenol A, perfluoroalkyl substances, and heavy metals disrupt hormonal pathways, with long-term health implications. Advances in biomonitoring, mechanistic studies, and NAMs are enhancing our understanding and risk assessment of these exposures. Continued interdisciplinary research and policy actions are critical to mitigate risks and safeguard public health.

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