



Enzyme-Disrupting Chemicals as the Elephant in the Room for Infertility

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Endocrine-disrupting chemicals (EDCs) are defined as “Exogenous compounds or mixtures that alter function(s) of the endocrine system and consequently cause adverse effects in an intact organism, or its progeny, or (sub) populations” [1].

The term “endocrine disruptor” was first proposed 30 years ago and the US Environmental Protection Agency has now identified 1,482 man-made chemicals that are considered EDCs [2].

EDCs have adverse effects on various steroid-sensitive tissues, thereby causing diseases such as obesity, diabetes mellitus, cardiovascular diseases, reproductive disorders, and cancers. Among these, particular attention has been paid to the male and female reproductive system and infertility in recent years. There are increasing number of manuscripts in various journals over the years on infertility and EDCs, where EDCs affect fertility either directly or indirectly.

Bisphenol A, steroid sex hormones, metal complexes, personal care products, pharmaceutical residues, flame retardants, and pesticides are examples of EDCs in day-to-day life. The mechanisms of EDCs involve divergent pathways including estrogenic, antiandrogenic, thyroid, peroxisome proliferator-activated receptor gamma, retinoid, and actions through other nuclear receptors; steroidogenic enzymes; neurotransmitter receptors and systems; and many other pathways. Epigenetic modifications can ensure the passage through next generations as well [1].

Route of human exposures to EDCs can be ingestion, inhalation or dermal contact through food, water, air and dust, and soil.

The male reproductive toxicity includes testicular damage, reduction in testosterone levels, prostatic hyperplasia and inflammation, and reduction in sperm quantity. The female reproductive toxicity includes increased estrogen levels, cycle irregularity, premature menopause, ovarian damage, and reduction in fertility. Early puberty among girls depends on so many factors including nutrition, stress, and ethnicity, and recently EDCs. Such estrogenic compounds are also associated with uterine fibroids, adenomyosis, endometriosis, endometrial cancers, and sub-fertility in humans. Pre- and periconceptional exposure to EDCs can cross various generations through the womb [3].

COVID-19 is a virus but mimics EDCs very closely. Obesity, adipose tissue cross talk, cardiovascular diseases, endocrine disorders, and malignancies have been implicated which affect fertility adversely.

The DES disaster illustrates three core principles of endocrine disruption. First, latency between exposure and effect can be extremely long, even decades. DES-exposed babies were born healthy by all appearance, with no evidence of the reproductive consequences that would ultimately befall them. The second key principle is that the timing of exposure, perhaps even more than dose, drives the potential and severity of adverse outcomes. The third key principle of endocrine disruption is that the dose response of many hormones and EDCs appears to be nonlinear, and adverse outcomes might be different at low vs high doses [4, 5].

Every pregnant woman on the planet is currently carrying a mixture of chemicals during her pregnancy that could affect not only her daughter’s reproductive health and fertility but also her granddaughter’s fertility which is a major reason why the topic of endocrine disruption must continue to receive global attention from scientists, governments, and the general public [6].

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References

1. Diamanti-Kandarakis Evanthia, et al. Endocrine-disrupting chemicals: an Endocrine society scientific statement. *Endocr Rev.* 2009;30(4):293–342. <https://doi.org/10.1210/er.2009-0002>.
2. Segal TR, Giudice LC. Before the beginning: environmental exposures and reproductive and obstetrical outcomes. *Fertil Steril.* 2019;112:613–21.
3. Hlisková H, Petrovičová I, Kolena B, Šidlovská M, Sirotkin A. Effects and mechanisms of phthalates' action on reproductive processes and reproductive health: a literature review. *Int J Environ Res Public Health.* 2020;17:6811.
4. Fowler PA, Bellingham M, Sinclair KD, Evans NP. Impact of endocrine disrupting compounds on female reproductive health. *Mol Cell Endocrinol.* 2011;355:231–9.
5. Kandaraki E, Chatzigeorgiou A, Livadas S, Palioura E, Economou F, Koutsilieris M, Palimeri S, Panidis D, Diamanti-Kandarakis E. Endocrine disruptors and polycystic ovary syndrome (PCOS): elevated serum levels of bisphenol A in women with PCOS. *J Clin Endocrinol Metab.* 2011;96:480–4.
6. Gore AC, Chappell VA, Fenton SE, Flaws JA, Nadal A, Prins GS. EDC-2: The Endocrine society's second scientific statement on endocrine-disrupting chemicals. *Endocr Rev.* 2015;36:1–150.

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