

## Everyday endocrine disruptors: challenges in investigation and interpretation



There is a growing body of epidemiological and toxicological literature focused on the effect of various substances and their disruption of endocrine function and contribution to female infertility. These chemicals are found in many commonly used and ubiquitous products and have been shown to exert effects on the hypothalamus, pituitary, ovaries, and uterus (1). Evidence also supports endocrine-disrupting chemicals that may contribute to male reproductive disorders (2).

Elsewhere in this issue, Beroukhim et al. (3) present the results of a retrospective, cross-sectional study in which the investigators analyzed data from the National Health and Nutrition Examination Survey along with urine triclosan (5-chloro-2-(2,4-dichlorophenoxy)phenol [TCS]) measurements from 2013–2016. The investigators report a 35% lesser likelihood of meeting criteria for infertility if levels of TCS were undetectable compared with those with detectable levels with a magnitude of association between TCS and presumed infertility increasing with the TCS concentration quartile (3).

Triclosan is used as a topical antimicrobial agent and has proven effective in the prevention of gingivitis when used in toothpaste (4). Although the United States Federal Drug Administration regulations have limited use and increased oversight for TCS in the last decade, it remains present in many over-the-counter products, including hand sanitizers, mouthwash, and toothpaste (4). In fact, TCS was detected in the urine of nearly 75% of participants in the 2003–2004 National Health and Nutrition Examination Survey (5). The investigators outline many potential mechanisms by which TCS exposure could contribute to endocrine disruption and therefore influence fertility, including at the level of the thyroid, endometrium, and ovary. Investigators also report other documented effects on menstrual regulation, follicular recruitment, and implantation.

Interestingly, respondents in this study who identified as Non-Hispanic Black or those with a history of smoking had a significantly lower level of urinary TCS, although the underlying cause for these differences remains unexplained. These 2 variables were controlled for in multivariable analyses; however, these identified but largely unexplained associations highlight the potential for residual, unknown confounding that may still bias these reported associations.

Furthermore, the use of a urine sample collected randomly, without a known time related to a period of infertility, in a population that included women beyond reproductive age limits the conclusions of this study. The half-life of TCS is only 21 hours; therefore, the use of urinary levels as a surrogate measure of long-term exposure may be limited.

Additionally, when the analysis was restricted to only those of reproductive age (aged 18–45 years), the significance of this association did not persist (3).

Studies like these highlight the challenges in studying the effect of environmental exposures on fertility, specifically the inability to control for all possible factors that may be associated with both exposure to certain endocrine-disrupting agents and infertility. Infertility is the result of many processes in both male and female patients, and disentangling the specific exposure that affects fertility is not easy. Exposure to other toxic substances, including other endocrine disruptors, may correlate with elevated urinary TCS levels and contribute to the identified associations in this study.

As health care providers and advocates for the safety and health of our patients, specifically those pursuing reproduction, we are challenged to interpret results like these for patients. Faced with an ever-growing list of seemingly ubiquitous substances that may exert effects on the many different layers of reproduction, alongside a deluge of consumer products claiming to be “clean” and “toxin-free,” it is important to refer patients to practical and evidence-based resources such as those from the Endocrine Society, the Environmental Working Group, and the Pediatric Environment Health Toolkit from the University of California at San Francisco.

Only with contributions like this article by Beroukhim et al. (3) will we continue to learn more about endocrine disruptors and strive for the safest possible environment for all people, especially those pursuing pregnancy.

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<https://doi.org/10.1016/j.xfre.2022.07.003>

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