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Reproductive disorders

Chemicals in the environment and human male fertility

Nicolas Olea, Mariana F Fernandez

Study shows that progressive replacement of some chemical components may have a beneficial effect on semen quality

In an article published in this issue ***(see page 467)***, Luc Multigner and colleagues[1] show that male exposure to short-chain glycol ethers has long-lasting negative effects on semen quality. Occupational exposure to chemicals in the workplace and their effects on testicular functions and male fertility is not a novel observation. Over the past few decades, investigations into the professional exposure of men have provided convincing evidence on the association between exposure to particular types of chemicals and male reproductive disorders.[2] This study reveals that precautionary measures focused on the progressive replacement of some chemical compounds by others may have a beneficial effect on semen quality.

In contrast to the relative consensus achieved around occupational chemical exposure, strong disagreements have arisen between supporters and opponents of the role of environmental chemicals in the decline in sperm production and quality observed in several regions of the world.[3] Environmental pollutants are known to exert adverse physiological effects by disrupting normal endocrine function (endocrine disruptor hypothesis), among other mechanisms.[4] Male conditions potentially related to exposure to endocrine disrupting chemicals include poor semen quality, low sperm count, low ejaculate volume, high number of morphologically abnormal sperms and low number of motile sperms as well as testicular cancer, reproductive organ malformations (for example, undescended testes, small penis size and hypospadias), prostate diseases and other abnormalities of male reproductive tissues.[4]

To date, conflicting results of epidemiological studies have failed to confirm the hypothesis that exposure to environmental chemicals with endocrine disrupting properties is associated with human reproductive health problems. Investigation of the link between exposure and effect is hampered by the complexity of the chemical mixtures present in the environment, both in terms of the numbers of compounds and the mechanisms by which they can affect fertility. Moreover, there is inadequate knowledge on the effects of chronic exposure to low levels of and combinations of chemicals, and on the relation between exposure in early development and its impact on adult life. Concerns about this relation have been heightened by indications from laboratory animal studies of specific windows during development that are especially sensitive to the effects of environmental chemicals.[5]

Inconsistencies in epidemiological findings may also have been caused by differences in the populations or ethnic groups studied, variability in the sensitivity of chemical analyses or failure to adequately control for potential confounders, effect modifiers, or other associated covariates. Chemicals may also interact with environmental, dietary, lifestyle, genetic susceptibility and reproductive factors that are not systematically measured across studies.[6] More importantly, a hypothetical association between environmental chemicals and human male fertility cannot be tested on the basis of individual compound levels, and account must also be taken of possible interactions among chemicals.[7] Interactions among multiple chemicals and endogenous hormones and their natural ligands may impair the internal homeostasis of the endocrine system, causing population-wide reproductive problems, such as lowered sperm counts in men.

Large-scale studies based on cohorts derived from the general population are needed to address this issue, with adequate numbers of participants in well-defined groups, allowing identification of the different levels of sensitivity of individuals to endocrine disrupting chemicals and estimation of inter- and intra-individual variations.[8] Elucidation of the relation between chemical exposure and disease also requires a rigorous approach to be adopted by human epidemiological studies: (1) classifying exposure by means of direct measurements rather than crude proxies; (2) taking account of the highly heterogeneous chemical classes implicated; (3) using well-designed biomarkers to quantify the combined effect of environmental mixtures and differentiating their effects from those of endogenous hormones; and (4) interpreting complex non-monotonic dose-effect relations.[9]

Many clinicians remain sceptical about the real impact of environmental chemicals on human health. Nevertheless, there is a need for physicians to contribute to our understanding of the health problems that arise from interaction between people and environmental chemicals. Thus, new clinical research should focus on constructing databases on male reproductive effects and exploring the mechanisms underlying male disorders, with a view to developing improved biomarkers and screening tools for use in medical practice. Moreover, exposure assessment should be incorporated as a routine component of patient examinations in the clinical setting.[10]

Finally, given the complexity of the environmental hypothesis, the compelling data gathered from animal studies, the uncertainty about cause-effect relations in humans and the slow pace of preventive measures, the precautionary principle should underlie policies and decision-making to expedite prevention-oriented public health strategies. The precautionary principle represents a courageous but necessary approach to weighing scientific evidence and making decisions in the face of uncertainty.

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