Toxicology in Reproductive Endocrinology

Roohi Jeelani, MD[a,*], Martin H. Bluth, MD, PhD[b,c], Husam M. Abu-Soud, PhD[a]

KEYWORDS

• Infertility • Reproductive outcomes • Subfertility • Toxicology • Alcohol • Drugs
• Environmental exposure • Health consequences

KEY POINTS

- Fertility relies on a series of time-dependent events, which are regulated by hormones. These hormones can be altered through exposure of consumed and environmental toxins.
- Reproductive dysfunction and infertility require laboratory evaluation, which involves serum hormone measurements.
- Infertility can be treatable through various assisted reproductive technologies. These can involve retrieval of the oocytes and insemination with sperm; however, if oocyte quality itself is disrupted through exposure through toxins, there is little that can be done to improve the quality.
- There are many toxins, including environmental, prescribed and illicit that can alter reproduction in the parent as well as future generations in a dose dependant manner.
- Currently there are no guidelines on laboratory testing for illicit drugs, alcohol, or environmental toxins in the scope of fertility testing. The best method remains to counsel and explain to patients at the first visit what impact it may have on their fertility.

INTRODUCTION

Reproduction is a dynamic process involving multiple pathways and signals throughout the body. If any of these steps are dysregulated, it can potentially lead to infertility. Many toxins and illicit drugs can impact and alter any part of these pathways, leading to difficulty in conceiving. Drugs such as opiates or cocaine have been known to disrupt oocyte quality, impacting fertilization and eventual fetal development and even childhood. Indeed, during in vitro fertilization, one may use genetic screening to biopsy and test the embryo for any chromosomal abnormalities, but other than that there is no laboratory test to detect the damage certain toxins may have caused. The

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[a] Department of Obstetrics and Gynecology, The C.S. Mott Center for Human Growth and Development, Wayne State University School of Medicine, 275 East Hancock, Detroit, MI 48201, USA; [b] Department of Pathology, Wayne State University School of Medicine, 540 East Canfield, Detroit, MI 48201, USA; [c] Consolidated Laboratory Management Systems, 24555 Southfield Road, Southfield, MI 48075, USA
* Corresponding author.
E-mail address: rjeelani@med.wayne.edu

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best and only intervention remains to consult patients at their first prenatal or even a preconception visit to discourage and eliminate potential exposure to any harmful toxins, drugs, or alcohol exposure because it may lead to detrimental effects on the fetus and even into adulthood for the child.

TOXICOLOGY AND REPRODUCTION

Behaviors such as illicit drug use, alcohol consumption, cigarette smoking, and excessive caffeine intake can alter reproductive health and fetal outcomes. Although the association remains loose and unclear, it is thought to be through the derangement of hormonal homeostasis and deterioration of oocyte milieu. In addition, toxin exposure to a variety of naturally occurring or man-made chemicals can alter hormone levels, resulting in an alteration in reproductive potential and possible fertility. Indeed, exposure to these toxins and its consequences are still not well understood, and many gaps still persist. As of yet, there are no guidelines regarding testing for these substances and at what level if any they can have an impact on reproduction. The optimal method to prevent any adverse effects on reproduction still remains to advise patients early on in their care to completely eliminate any substances of abuse and prevent any exposure to potential harmful toxins.

Illicit Drugs

Approximately 60% to 80% of adults use alcohol, and in addition to that, approximately 10% of adults may suffer from some type of substance use to the point of addiction.[1] In many instances there appears to be even higher rates of substance abuse as seen with analysis of meconium samples from newborns. Previously published studies, in certain cohorts, showed that neonates were 31% positive for cocaine, 18% positive for opiates, and 17% positive for cannabinoids, and out of these, many of them were positive for more than one of these drugs.[2,3] It becomes difficult to point to one drug to precipitate a certain outcome because many patients are multidrug abusers as noted by the study of meconium. Opiate and cocaine use while pregnant can lead to neonatal abstinence syndrome, which can persevere for months and lead to increased risk of neurobehavioral disorders and altered central nervous system (CNS) function later on.[4]

In women, the strongest evidence of the adverse impact of cocaine on reproduction is demonstrated by adverse obstetric outcomes, which include early and late pregnancy loss and placental abruption. Reproductive disturbances in substance-abusing adult women are evidenced by menstrual abnormalities, which predominantly consist of amenorrhea in heroin abusers.[5] On the contrary, the fact that many of these women who are regular narcotic abusers achieve pregnancy and deliver implies that the degree of reproductive insult is not enough to prevent the birth of an exposed and affected baby. However, use of narcotics in women who were on the edge of being infertile may push them into the infertility zone. Previous work has established that in adult mammals opiates bind in the hypothalamus and cause inhibition of the secretion of luteinizing hormone (LH), which can lead to mild to moderate gonadal suppression.[6,7] Not only that, but these drugs can impact fertility; however, it remains difficult to attribute a particular outcome to the use of a certain drug. Drug dependence can lead to varying effects, including malnutrition, increased risk of infectious diseases, poor health care, and poor pregnancy outcomes. These patients also have increased risk of physical and verbal abuse, which also affects the probability of successful fertility and fetal health. People addicted to drugs may be so compromised that the steps essential for normal reproductive hemostasis will be adversely affected leading

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