Do some addictions interfere with fertility?

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Management of infertile couples should focus on the effects of their professional environment and quality of life, such as stress, smoking, alcohol, weight, diet, and the use of electronic devices. It should also focus on reducing these negative factors and improving the couples' quality of life in conjunction with assisted reproduction treatments. The challenge for human reproduction now, and in the decades to come, is to introduce the concept of "ecofertility" in our practices. Early education and prevention are essential to preserve fertility. (Fertil Steril® 2015;103:22–6. ©2015 by American Society for Reproductive Medicine.)

Key Words: Infertility, toxic factors, assisted reproductive techniques (ART), lifestyle, prevention

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The causes of infertility have changed significantly over the past 30 years, and the impact of environment and lifestyle on the difficulties experienced by couples plays an important role in fertility alteration. Recording of these factors began about 10 years ago (1, 2).

The fertility of a generation would appear to be linked to toxic factors, the activity of which began during the intrauterine life of the mother, i.e., pollutants, which seem to act as endocrine disruptors, especially on male fetuses, and other behavior-dependent toxic factors, such as smoking, alcohol, and lifestyle. Fertility in adults may be altered by factors such as cannabis, antidepressants, weight, diet, profession, intense exercise, stress, sexual intercourse targeted at the date of ovulation, and infertility-related stress (3).

Infertility-related toxic factors and lifestyles are still often not detected and the diagnosis and early treatment of these problems would enable natural fertility to be improved and would reduce the need for medically assisted procreation. They would also reduce the complications associated with the latter (4) by producing spontaneous pregnancies without the need for major procedures (5).

FACTORS THAT MAY INFLUENCE THE FERTILITY OF COUPLES AND ARE CONTINGENT UPON LIFESTYLE

Smoking

Tobacco. In women, the Augood et al. meta-analysis (6) shows that smoking generates a delay in conception of more than a year. This is both dose and duration dependent for the exposure. There is double the risk of being infertile, reduction in ovarian reserve, and a lower level of antimüllerian hormone (AMH), as well as short irregular cycles, greater ovarian insufficiency, and dysmenorrhea in the group of smokers (7). Products contained in tobacco, i.e., cotinine, cadmium, and oxygen peroxide, can be found in follicular fluid with an alteration in oocyte meiotic resumption. Hydrocarbons present in tobacco interact with the aryl hydrocarbon receptor, which activates apoptosis causing ovotoxicity (8) and increased onset of ovarian insufficiency.

In men, during the antenatal period maternal exposure to tobacco has an impact resulting in an increased risk of bilateral cryptorchidism, a 20% decrease in the total number of spermatozoa in the adult male children of women who smoked more than ten cigarettes per day (9), and a reduction in testicular volume (10). Tobacco consumption by adults affects erectile function and increases chromosomal aberrations in the spermatozoa, causing an increase in the number of miscarriages.

Although the direct action of tobacco is not well understood, stopping smoking for 3 months allows sperm quality to improve: 72 million versus 29 million per ejaculate, 79% motility versus 33%, 20% versus 60% necrotized, and 23 million grade A spermatozoa count after swim-up per ejaculate versus 3 million (11).

The negative impact of smoking during pregnancy is a cause for concern to researchers, owing to the likelihood

Received September 9, 2014; revised October 31, 2014; accepted November 4, 2014.
S.A. has nothing to disclose.
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Fertility and Sterility® Vol. 103, No. 1, January 2015 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2014.11.008

of the future fertility of children exposed in utero being compromised. Recently, Sobinoff and al. (12) showed in a mouse model that maternal exposure impairs the fertility of male offspring. Pregnant women should be given as much information as possible.

In assisted reproductive technology (ART) cycles, studies have shown that, in both men and women, smoking causes a reduction of >40% in their chances of successful ART and an intracytoplasmic sperm injection (ICSI) failure rate three times higher than in nonsmokers. Furthermore, the risk of not conceiving during IVF/ICSI is four times higher in those who smoked for >5 years (13).

It would appear that female smokers have a lower level of E_2 during ovarian stimulation, fewer oocytes and embryos are obtained, and there is also a probable increase in the thickness of the oocyte zona pellucida (14).

Stopping smoking is essential, at least while a pregnancy is planned, to halt the negative effect on ovarian function and increase the chances of spontaneous pregnancy.

Marijuana. In men, consuming cannabis several times a week for 5 years causes a reduction in the volume and number of spermatozoa and changes in morphology and motility, with sperm hyperactivity and reduction in their fertilization capacity (12). Cannabis is eliminated very slowly compared with tobacco, and the harmful effects are more significant. Marijuana reduces T production, with more than one-third of consumers presenting oligospermia. Marijuana also causes reduced libido, gynecomastia, and erectile disorders (15).

Marijuana contains the delta-9-tetrahydrocannabinol (THC) cannabinoid, which blocks the release of GnRH from the hypothalamus and LH production by the adenohypophysis. THC activates the endocannabinoid receptors, thus producing abnormalities in acrosome reaction and a reduction in sperm motility (15). In the testis, marijuana reduces T production and interferes with spermatogenesis. In nonhuman animal models, chronic administration of THC impairs spermatogenesis at both mitotic and meiotic stages, with mature sperm showing severe morphologic defects. These findings are mirrored in humans, with more than one-third of chronic marijuana users having oligospermia.

Although human studies are scarce, and those that do exist are limited by their observational nature, the available evidence substantiates the claim that marijuana use, whether illicit or prescribed, has a detrimental effect on male reproductive potential. In women, a disturbed menstrual cycle, a reduced number of oocytes harvested during in vitro fertilization, and a higher risk of prematurity have been observed (16).

Cohort studies are required, but current studies show that marijuana has a negative effect on fertility. There is no fundamental evidence about the direct effects of THC on ART cycles.

Alcohol

The available information on the potential effects of alcohol is less clear, particularly because of the diversity of alcoholic drinks available and the difficulty in determining a threshold consumption frequency. In men, the risk threshold for an impact on male infertility would appear to be 30 g alcohol per day, e.g., three glasses of wine (17). Excessive alcohol consumption has been suggested as a risk factor for male infertility.

Studies (18) have demonstrated that ethanol has an effect on the hypothalamus, where it blocks the secretion of GnRH and the binding of the GnRH precursor, pre–pro-GnRH, to a functionally active GnRH hormone. This process results in a reduction in both LH and FSH, with subsequent spermatogenic impairment.

Recently, Jensen et al. (19) showed a significant increase in serum free T with increasing alcohol consumption in the week preceding the visit to the IVF center. That study suggested that even modest habitual alcohol consumption of more than five units per week had adverse effects on semen quality. The most pronounced effects were seen in men who consumed more than 25 units per week. Alcohol consumption was also linked to changes in T and SHBG levels. The alcohol threshold level required to affect semen adversely remains unclear. Nevertheless, young men and men undergoing ART cycles should be advised to avoid habitual alcohol consumption.

In women, moderate consumption of wine (more than two glasses per day) appears to reduce the time taken to conceive. As regards ART cycles, studies are quite scarce (20). Wdowiak et al. (21) showed that alcohol consumption may cause the development of embryos of inferior quality. Significantly more class B embryos came from oocytes of women who consumed alcohol, compared with class A embryos. In that study, 42.59% of the women consumed alcohol. Prevention of alcohol consumption among women of reproductive age should be promoted to safeguard their fertility and future motherhood.

Medications

Many medications have been associated with an alteration of fertility in men and women (22). These include some antihypertensives (calcium antagonists), chemotherapy, radiotherapy, and treatments for neuropsychiatric diseases (antidepressants) and stomach ulcers (23). Amory and Swerdloff (24) recently implicated dutasteride and finasteride (hair loss treatments) as contributing factors for infertility in men. Conclusive literature on the medications and their effects on fertility remain insufficient. More information on medications should be sought from infertile patients during consultation.

Caffeine

The mechanism of the effect of caffeine on fertility is unknown. In men, Belloc et al. (25) found that 75.6% of men drank coffee (3.0 ± 1.8 cups/d). Among caffeine consumers, semen volume was slightly higher (3.2 ± 1.6 mL vs. 3.1 ± 1.6 mL; $P<.01$) for the pH ($P<.01$), but concentration was lower (60.0 ± 90.7 million/mL vs. 69.6 ± 124.9 million/mL; $P<.01$). No relationship was observed for motility and morphology, or for DNA fragmentation and chromatin decondensation. In a multivariate model including age, results were confirmed for volume ($P<.01$), but not for