

Smoking & Infertility
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To smoke or not to smoke?

Well, let me cut to the chase: If you are trying to conceive, no matter what the cause of your infertility is, you're better off staying away from that cotinine!

According to a US Surgeon General, cigarette smoking is "the chief, single, avoidable cause of death in our society and the most important public health issue of our time." Cigarette smoking kills approximately 434,000 Americans each year. These deaths are directly linked to smoking-related disorders such as cancer, heart disease, and chronic respiratory ailments. Among women of reproductive age, 29% smoke. Of these women who become pregnant, between 19% and 30% continue to smoke. The health risks of smoking include decreased estrogen levels, leading to osteoporosis and an increased risk of cardiovascular disease, especially among users of oral contraceptives, an increased risk of infertility and of complications during pregnancy, an increased risk of miscarriage and stillbirth, a greater incidence of low birth weight in offspring, an increased risk of sudden infant death syndrome in offspring, a greater risk of cervical cancer, and an increased incidence of ectopic pregnancy.

Although infertility can be caused by many different factors, most infertility is caused by abnormal oocytes and/or sperm production, tubal defects, or endometriosis. It is important to note, however, that a significant proportion of infertility is unexplained. Investigators hypothesize that environmental factors have the potential to alter male and female reproductive tissues and thus affect the ability of couples to conceive healthy offspring.

A nice review of this topic done by Hruska et al in 2000 clearly summarized this issue. "To date, most studies of environmental exposures and reproductive function have focused on the association between cigarette smoking and infertility and subfecundity. Individuals may be exposed to the toxicants in cigarette smoke through both active and passive smoking. An estimated 28 million men and 23 million women in the United States actively smoke cigarettes; it is further estimated that 60% of nonsmokers, including children, are exposed to tobacco smoke daily. At least 43 carcinogens and more than 300 polycyclic aromatic hydrocarbons have been identified among the 4,000 chemical constituents of cigarette smoke. In addition, tobacco smoke contains several other known toxicants, such as methyl isocyanate, benzene, acetone, ammonia, arsenic, butane, carbon monoxide, cyanide, dichlorodiphenyltrichloroethane (DDT), formaldehyde, lead, methanol, polonium 210, and naphthalene."

A systematic review of multiple articles found a consistent association between female smoking and impaired natural fecundity. In one meta-analysis, an OR for the risk of infertility in women smokers versus nonsmokers was calculated as 1.60 (95% confidence interval [CI]).

Several studies indicate that smoking negatively impacts the success of assisted reproductive technologies in women with infertility. Smoking within 1 month of oocyte retrieval in a retrospective study of 261 women undergoing their first in vitro fertilization treatment cycle significantly reduced the occurrence of clinical pregnancy, whereas past smoking increased the risk for cycle cancellation. In another retrospective study of 173 women undergoing consecutive in vitro fertilization-embryo transfer cycles, smokers required a higher mean number of human menopausal gonadotropin ampules per cycle than nonsmokers to achieve comparable clinical pregnancy rates. The women who smoked produced lower mean numbers of retrieved oocytes.

A study by Hull et al from England looked to determine whether passive as well as active smoking by women or smoking by men is associated with delayed conception. After correction for confounding factors, delayed conception was statistically significantly associated with both active smoking by the woman for > 6 months and for > 12 months and her exposure to passive smoking compared with women with no exposure to tobacco smoke. Heavy smoking by men was independently associated with delayed conception. In active smokers, the effect increased with the number of cigarettes.

Active smoking reduces female fertility in a dose-related manner. The odds that a smoking woman will conceive naturally have been reported to be reduced to around 80% of a nonsmoker; these odds vary with duration of attempts to conceive and amount smoked. Compared with nonsmokers, the odds that smokers will conceive naturally in a single cycle have been estimated to be reduced to 72%, and their odds of conceiving in a cycle of IVF are reduced to 66% on average.

Menstrual cycle function is closely linked with a woman's dependability or ability to become pregnant. It is well known that women, who suffer from irregular periods, whether short or long, do not have regular ovulatory cycles. The Agricultural Health Study is one of the largest studies whereby the medical and lifestyle factors associated with menstrual cycle characteristics among 3941 menstruating women were evaluated. Simply stated, cigarette smoking was associated with short cycles and irregular cycles. The odds of having irregular cycles was 3.6 among women who smoked more than a pack a day compared with nonsmokers.

Some studies have reported more frequent, short cycles among smokers or heavy smokers, although several studies did not find associations between

smoking and cycle length. Data from this study supports an association, with even moderate smokers having increased odds of short cycles. Women with irregular cycles were less likely to have ever been pregnant. It is likely therefore that exposure or risk factors that perturb normal menstruation also may increase a woman's risk of other reproductive disorders.

Possible mechanisms for the decreased fecundity in women include reduced oocyte fertilization and embryo cleavage during IVF treatment; this mechanism has been linked to the presence of cotinine, which is an index of nicotine and perhaps other smoking products that reach the follicle. Nicotine has adverse effects on steroidogenesis by the granulosa cells of the ovarian follicle that support the oocyte. Accelerated loss of primordial follicles is suggested by advancement of the menopause by about 2 years; premature increase in circulating levels of follicle-stimulating hormone; and reduced ovarian responsiveness to stimulation with exogenous gonadotropins. Another effect on the chance of natural conception is suggested by reduced ciliary activity of the oviductal mucosa found in animal experiments.

Most subfertile men have no definable cause for their condition; only in approximately one-fifth can a clear cause be determined. Despite the significant contribution of the male factor to the infertile state of couples, relatively little has been done to increase our knowledge in this field. A study conducted in Singapore has demonstrated a clear association between smoking and male factor infertility. The study evaluated semen parameters in 218 men with no known cause for infertility and a total of 227 men whose spouses were pregnant at the time of the study were recruited as controls. Smoking was found to be a significant risk factor for infertility. Active smoking by men has also been associated with spermatozoal DNA fragmentation, axonemal damage in the tail, and decreased sperm count. In vitro exposure to cigarette smoke or to seminal plasma from smokers caused reversible inhibition of sperm motility.