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Effects of occupational solvent exposure on fertility

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Key terms carbon disulfide, ethylene glucol ethers, menstrual disorders, reproductive hazards, semen quality, styrene, tetrachloroethylene.

Organic solvents are among the most important occupational reproductive hazards. They are used widely in various fields of industry, and they have been related to several types of adverse reproductive outcomes. Human data on the effects of solvent exposure on male or female fertility are, however, scarce and divergent. Most studies have focused on maternal solvent exposure and pregnancy outcome, and the available evidence suggests that exposure to high levels of solvents increases the risk of spontaneous abortion (1). The findings on other pregnancy outcomes and the effects of paternal exposure are less conclusive, but suggest also that solvent exposure may represent a hazard to the developing fetus. This review focuses on the effects of occupational solvent exposure on fertility (occurrence of pregnancies) and some biological processes that may affect fertility, such as menstrual function, semen characteristics and hormone levels (table 1).

Overall solvent exposure

The effect of overall solvent exposure on fertility has been examined in 3 epidemiologic investigations. Two of them were conducted among workers biologically monitored for solvents (2, 3). Exposure was assessed on the basis of the study subjects' own work descriptions and on biological exposure measurements. The results indicated prolonged time to pregnancy for women with daily or high exposure to solvents (2). However, among men the association between solvent exposure and fertility was weak. Time to pregnancy was only slightly and insignificantly prolonged in the wives of men exposed to high and low or intermediate levels of solvents (3).

In a third study, based on clinical patients, women medically diagnosed as infertile were compared with postpartum women with a normal birth. Infertile women were found more likely to report exposure to solvents

than fertile women (4). The analysis by medical diagnosis of infertility showed an increased risk for ovulatory dysfunction, tubal-factor infertility, and endometriosis. This study has, however, been criticized because of its potential for selection bias and the high likelihood of recall bias, since exposure assessment was based on self-reported data.

Ethylene glycol ethers

Ethylene glycol ethers and their acetates have been used in a variety of industries (eg, photography and dyeing, silk screen printing, manufacturing of electronic components) and products (eg, varnishes, paints, resins, thinners, and cleaners). Recently, the effects of these agents

Table 1. Occupational solvent exposure associated with adverse effects on fertility.

Exposure, industry	Effect
Women	
Overall solvent exposure, various industries	Reduced fertility, infertility
Carbon disulfide, viscose rayon industry	Menstrual disorders
Ethylene glycol ethers, semi-conductor industry	Reduced fertility, menstrual length variability
Styrene, plastics industry	Menstrual disorders
Tetrachloroethylene, dry cleaning	Reduced fertility, infertility, menstrual disorders
Toluene, shoe industry, various industries	Reduced fertility, menstrual disorders
Men	
Carbon disulfide, viscose rayon industry	Reduced libido and potency
Ethylene glycol ethers, semi-conductor industry	Decreased sperm count, oligospermia
Styrene and acetone, reinforced plastics industry	Sperm anomalies
Tetrachloroethylene, dry cleaning	Subtle changes in semen quality
Toluene, printing industry	Decreased gonadotropin hormone levels

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have been the focus of growing interest, since their adverse reproductive effects, including infertility, have been well documented in animals. In a study on female semiconductor manufacturing workers, the potential for exposure to mixtures containing ethylene glycol ethers was related to an increased risk of subfertility, defined as taking more than 1 year to conceive (5). In another study, women were followed by daily urine samples to confirm pregnancies, and especially early fetal losses. The results showed reduced fecundability among the semiconductor workers exposed to these agents, but the number of exposed women was very small (6). No clear differences were observed in menstrual cycle characteristics between exposed women and their referents. The variability in menstrual cycle length was, however, increased in women working in photolithography, which involves potential exposure to organic solvents, including glycol ethers (6).

Exposure to 2-methoxyethanol and 2-ethoxyethanol has been associated with reduced sperm count and an increased prevalence of oligospermia and azospermia in shipyard painters. A lower sperm count has also been observed in workers of a metal-casting company exposed to 2-ethoxyethanol, although no effect of exposure on other parameters of sperm morphology or function was detected (7). No clear association was noted between exposure to ethylene glycol ethers and subfertility or reduced fecundability in male semiconductor workers (5, 6).

Styrene

Exposure to styrene is common in the reinforced plastics industry. The results of the studies on styrene exposure and menstrual function have been conflicting. Some early studies reported high frequencies of menstrual disturbances in styrene-exposed women, but the methodological shortcomings of these studies limit the interpretation of their findings. More recent investigations have revealed no difference in menstrual function between exposed and unexposed workers (8). Neither was there an association between male or female exposure to styrene and reduced fertility (2, 3). One study found, however, a higher prevalence of childless couples in an exposed versus an unexposed group, but owing to the small sample size some potential confounders could not be dealt with adequately (8).

The results on the effects of styrene on sperm quality are conflicting (9). An increased proportion of sperm with abnormal morphology was observed for men exposed to styrene and acetone, but no differences in other sperm parameters or gonadal hormones were seen. Overall, there is no clear evidence on the adverse effects of styrene on male or female fertility, although the possibility of an effect at high exposure levels cannot be excluded.

Tetrachloroethylene

Tetrachloroethylene is mainly used as a dry-cleaning agent and a degreaser. Dry-cleaning work with potential for exposure to tetrachloroethylene has been associated with an increased frequency of menstrual disorders, infertility and delayed conception in women. A time to pregnancy study suggested also decreased fertility in a small group of women exposed to tetrachloroethylene in dry cleaning (2). Among men subtle changes in semen quality have been reported from exposure to this agent. There is also weak evidence suggesting that it may take the wives of men exposed to tetrachloroethylene slightly longer to conceive (3, 9). Although the data on the effects of tetrachloroethylene exposure are limited, they suggest a possible association between exposure and reduced fertility, particularly among women.

Carbon disulfide

Carbon disulfide is a solvent used primarily in the production of viscose rayon. Disturbances in sexual function, such as decreased libido and potency, have been reported in several studies on male workers exposed to carbon disulfide. The study findings on other reproductive effects of carbon disulfide are equivocal. Adverse effects have been reported for men chronically poisoned with carbon disulfide; at lower levels of exposure, however, no significant alterations in semen quality or decreases in fertility were noted (10). The results on the effects on gonadal hormones have also been inconsistent. In women, menstrual disorders, including irregular cycles and unusual bleeding, have been related to carbon disulfide exposure.

Other solvents

Other solvents linked with menstrual disturbances include benzene, 2-bromopropane, formaldehyde, toluene and xylene. Reduced fertility has been observed in shoe factory workers exposed to solvents, such as toluene, hexane and acetone (2). In men, some alterations in semen quality have been reported for exposure to trichloroethylene and methylene chloride. Toluene exposure has been related to decreased gonadotropin hormone levels (9).

Conclusions

Overall, evidence of the adverse effects of solvents on female or male fertility is scarce and inconclusive. Many studies suffer from methodological shortcomings, such as small sample size, low participation rates, potential for selection bias and potential for misclassification of exposure. Coincident exposure to several agents makes it also difficult to ascribe adverse effects to a specific compound. The epidemiologic evidence on the effects of exposure to solvents in general as well as studies on some individual solvents suggest, however, an association

between solvent exposure and reduced female fertility. The studies show only weak associations between solvent exposure and decreased fertility among men, although exposure to some specific types of solvents has been related to semen abnormalities, disturbances in sexual behavior, and hormonal imbalance.

The findings of human studies on sperm abnormalities and increased subfertility in women, and suggestively in men exposed to ethylene glycol ethers, are consistent with the results of animal experiments indicating the reproductive toxicity of these agents. Carbon disulfide seems also to have some harmful effects on male reproductive function, mainly on libido and potency. Data on the effects of tetrachloroethylene exposure on women in dry cleaning is limited but consistent, suggesting an association between exposure and reduced fertility. The paucity of data on the associations of other individual solvents with fertility, menstrual function, semen characteristics or hormonal levels precludes the drawing of firm conclusions.

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