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Genotoxic Effects of Smoking on Human Gametes and Embryos

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Tobacco smoking adversely affects reproductive function. Epidemiological studies have shown consistent, dose-related associations of smoking with delay of conception, increased risk of abortion, and early age of menopause. Recent investigations have been aimed at understanding these deleterious effects of smoking. Reproductive technologies have been useful for providing clinical data on reproductive outcome and biological material such as reproductive fluids, spare oocytes, spermatozoa, and spare early embryos.

Components of cigarette smoke, such as cadmium (a heavy metal), nicotine (a toxic alkaloid) and its metabolite cotinine, were detected in dose-relationship with smoking in ovarian granulosa cells, and in follicular fluids and seminal plasma. This gonadal environment in smokers has been shown to be detrimental to the development and viability of their gametes; furthermore, it induces genetic damage. Heavy female and male smoking is associated in dose-relationship with *i*) reduced numbers of retrieved oocytes (by 8% to 17%); *ii*) reduced density of ejaculated spermatozoa (by 13% to 18%); *iii*) alterations in the meiotic spindle leading to chromosomal errors in oocytes (diploidy) and in spermatozoa (aneuploidy). In oocytes of mice exposed during meiotic maturation *in vitro* to nicotine or cadmium, severe alterations of meiotic spindle structure and chromosome alignment were also found.

Benzo(a)pyrene [B(a)P], a carcinogenic polycyclic aromatic hydrocarbon, is produced from cigarette combustion. Its reactive metabolite binds covalently to DNA, forming adducts. B(a)P-DNA adducts were detected, in elevated levels, in ovarian granulosa cells of smoker women, in spermatozoa of smoker males, and in preimplantation embryos of smoking couples. Transmission of DNA-adducts to embryos was found to be mainly by sperm. This may be related to many divisions occurring in spermatogenic cells and/or to a low capacity of mature spermatozoa to repair prezygotic DNA damage.