CHILDHOOD CANCER

A chilling conclusion

The conclusion reached by Chica and colleagues from their prospective study of the effects of smoking during pregnancy is that maternal smoking is associated with increased chromosomal instability in the fetus, including chromosomal changes that have been implicated in infant leukaemia.

Although many studies have examined the effects of smoking on the developing fetus, they have used surrogate tissues such as maternal serum, blood cells obtained after birth or placental chorionic villi to show increases in DNA damage. Chica *et al.* instead examined amniocytes, which are representative of the fetus itself, so chromosomal abnormalities detected here would determine the extent to which exposure to tobacco smoke *in utero* directly affects the developing child.

In a bid to rule out other factors known to induce chromosomal damage, the authors undertook a painstaking set of interviews to identify women who required a routine amniocentesis for prenatal diagnosis but who did not drink tea, coffee or alcohol. From these women, the authors recruited 50 healthy pregnant women, half of whom had smoked for at least the past 10 years and had continued to smoke during pregnancy, and half of whom had never smoked and were not exposed to passive smoking. Maternal age was, by chance, higher in the smoker group, but careful statistical analysis by the authors indicates that the age difference does not significantly affect the findings of the study.

Using the amniocytes from each amniocentesis, Chica and co-workers analysed 100 metaphase chromosome spreads for chromosomal lesions or abnormalities. Although evidence of genomic instability was found in both groups, the incidence of structural chromosomal abnormalities was significantly higher in amniocytes that are obtained from pregnant smokers (12.1%) compared with never smokers (3.5%).

The detailed cytogenetic analysis in both groups showed that the chromosomal breakpoints were non-random and correlated with known fragile-site bands. Specifically, chromosome regions 5q31, 17q21 and 11q23 were more often affected in smokers than never smokers and regions 5q31.1 and 11q23 correspond to known fragile sites. Interestingly, previous reports have indicated that exposure to tobacco smoke increases fragile-site expression and chromosomal instability *in vivo*, and that this can contribute to tumour formation.

A high proportion of infants (40–60%) with leukaemia have rearrangements in 11q23, and some researchers have suggested that this rearrangement occurs *in utero*. The authors finding supports this hypothesis, and given that the genes *ATM*, *PLZF* and *MLL*, which are all associated with the development of leukaemia, are located within 11q23, further studies are warranted. However, large epidemiological studies are needed to determine whether the offspring of smokers have an increased lifetime risk of cancer.

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References and links

ORIGINAL RESEARCH PAPER Chica, R. *et al.* Chromosomal instability in amniocytes from fetuses of mothers who smoke. *J. Am. Med. Assoc.* **293**, 1212–1222 (2005)