Re: Early Age at Smoking Initiation and Tobacco Carcinogen DNA Damage in the Lung

It is clear from the analysis by Wiencke et al. (1) that an earlier age at smoking initiation is associated with a greater frequency of DNA damage. It should also be clear that children of parents who smoke are more likely to begin smoking at a younger age than are children of nonsmoking parents. This conclusion suggests the possibility that a portion of the susceptibility to DNA aduct formation observed in those with the youngest age at initiation of smoking might have been inherited from their parents’ damaged DNA. Should not the parents’ smoking history be included as one of the factors in the multivariate analysis?

JOHN H. GLASER

REFERENCE


NOTE

Correspondence to: John H. Glaser, 4 Woodpark Circle, Lexington, MA 02421 (e-mail: GlaserJ@polaroid.com).

RESPONSE

Dr. Glaser raises the complex and thorny issue of the role of parental smoking in lung cancer risk among their offspring and suggests the possibility that genetic transmission of “tobacco-damaged DNA” through the germline may play a part in this risk. It is clear that children whose parents smoke are more likely to become regular smokers themselves. Recent studies show that the negative impact of parental smoking may operate long before the teen years, so that preventing experimentation and initiation of smoking requires intervention throughout childhood.

Leaving aside the possible infrequent occurrence of constitutional (germline) lung cancer genes, the association between smoking and lung cancer within families is likely due to acquired smoking behaviors that are shared by family members rather than to germline DNA damage. The strong evidence linking maternal smoking with low birth weight and respiratory problems, including SIDs (sudden infant deaths), is evidence of in utero toxicity from exposure to tobacco smoke constituents that is not heritable. In addition, transplacental transmission of potent tobacco carcinogens has been documented. For example, the urine of infants born to smoking mothers has been shown to contain metabolites of tobacco-specific nitrosamines (1). Consequently, among the most sensitive indicators of the possible influence of parental smoking in familial cancer is the occurrence of cancers in children whose parents smoke. Despite intensive study, maternal smoking has not been established as a risk factor for childhood cancers (2–4). On the other hand, chromosomal abnormalities (5) and DNA damage in sperm have been documented among smokers, and increased risks for certain childhood cancers have been associated with paternal smoking (6). Further study is needed, however, and it will remain a very difficult problem to determine whether associations are due to germline transmission of smoking-induced mutations rather than to in utero or postnatal exposures to tobacco smoke. The question of lung cancer and parental exposure, because of the later age of onset, is even more complicated.

In our study of ex-smokers with lung cancer (7), we reported that the DNA damage levels in lungs were greater in patients who reported an early age of smoking initiation. We did not attempt to factor in parental smoking, nor do we think it would be informative, in part for the reasons cited above, but also for the practical reason that our patients, whose mean age was 66 years, would not be able to consistently provide their parents’ smoking habits before their own birth. Most of the parents of our case subjects were deceased or unable to provide first-hand histories. The studies alluded to above on childhood cancers do not suffer from these limitations. Hence, although more research is needed on the mechanisms of tobacco damage in germ cells, we recognize that the dominant influence of parental smoking on lung cancer occurrence is in the uptake of the smoking habit. In addressing the responsibility of parents, the potential for blame and guilt must be minimized and each of us should be reminded of the strong addictive properties of nicotine.

JOHN K. WIENCZE

REFERENCES


NOTE

Correspondence to: John K. Wiencke, Ph.D., Department of Epidemiology and Biostatistics, School of Medicine, University of California San Francisco, 500 Parnassus Ave., MU-W 420, San Francisco, CA 94143-0560 (e-mail: wiencke@itsa.ucsf.edu).