Letter to the Editor

Correspondence re: A. W. Hsing *et al.*, Diet, Tobacco Use, and Fatal Prostate Cancer: Results from the Lutheran Brotherhood Cohort Study. Cancer Res., *50:* 6836–6840, 1990.

The conclusions drawn by Hsing *et al.* (1) in the article showing an association of cigarette smoking with fatal prostate cancer must be viewed with some skepticism. Although the authors discuss the limitations of the study, a closer examination of the methods and results suggests that cigarette smoking is not an etiological factor. In any cohort study, it is desirable to follow the cohort to watch for changes in risk factor prevalence. As pointed out by the authors, 40% may have quit smoking in the 20-year period following base-line measurements. Similarly, among those who continued to smoke, the majority would have switched from high-tar nonfiltered cigarettes to low-tar filtered cigarettes (2). Smoking inhalation patterns would have also changed. Smokers compensate for decreased tar by increasing puff volume, puff frequency, inhaling deeper, and increasing the number of cigarettes smoked per day (3). Temporal changes in prevalence and smoking behavior is a complex phenomenon, and is related to socioeconomic status, education, and occupation. Smoking patterns in 1966 are not a very good indicator of lifetime tar and other cigarette-related carcinogens. Misclassification may be nondifferential, but this is a very tenuous assumption.

The smoking data presented by the authors do not support an association. A statistically significant elevated relative risk is found only for ex-smokers or occasional smokers and not for current smokers. If anything, there seems to be an inverse dose response with increasing cigarettes per day. The failure to find a significant association is not due to small numbers but to small differences, as there are a huge number of person years followed. Even more striking is that only 3% of smokers were heavy smokers (>30 cigarettes per day). We have found that, even among hospital controls with non-tobacco-related conditions, 20–25% of smokers were heavy smokers. Among cases of tobacco-related cancers, approximately 45% of smokers were heavy smokers (4, 5). The authors should also examine the duration of smoking among ex-smokers. If recent quitters had the same age-adjusted risk as those who quit many years ago, as we suspect, this would also fail to provide evidence for an association with tobacco.

With regard to mortality as an end point, the role of cigarette smoking is not acknowledged. There is a large difference between the age-adjusted incidence and mortality of prostate cancer in the United States (95.1 compared to 24.2/100,000) (6). Those who die from prostate cancer are less likely to be health conscious and have periodic screening for prostate cancer than are survivors. This health consciousness might not be reflected in the base-line demographic variables. Thus, cigarette smoking in this study may be a correlate of mortality and not of incidence.

Another small but real limitation in this study is the reliability of death certificates. Although this would not normally pose a substantial problem in a cohort design, autopsy studies of the prostate in elderly males who died of other causes have revealed a high prevalence of occult adenocarcinoma (7, 8). The weak association and the lack of a dose-response relationship may be influenced by diagnostic misclassification.

The authors have also failed to cite a large, recent case-control study which found no evidence of an elevated risk for prostate cancer with cigarette smoking (9).

Assuming that the relative risks found in the study are accurate and represent a biological phenomenon, they would represent relative risks for high-tar nonfiltered cigarettes that are currently rarely smoked. If the reduction in lung and laryngeal cancer risk found among smokers who switched to filtered cigarettes also applies to prostate cancer risk, then the weak association found in this study has little bearing on prostate cancer for today's smokers. Efforts to uncover the etiology of this cancer should focus on metabolic parameters which can be measured in the laboratory such as endocrine and nutritional factors.

Received 11/26/90; accepted 3/21/91.

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