increase the risk of persistent HPV infection or cervical neoplasia. Other studies, however, have reported conflicting results. A study conducted among adolescent females in Canada reported no association between either smoking or oral contraceptive use and lower serum or red blood cell folate levels after controlling for folate intake, nor was smoking associated with lower serum B12 levels (3). Other studies have also reported no association between oral contraceptive use and levels of folate (4, 5). Furthermore, the majority of case-control studies of folate/vitamin B12 and cervical neoplasia have failed to find any association (6), and results from clinical intervention trials of folic acid do not suggest that folic acid supplementation alters the natural history of HPV infection (7, 8). Dr. Hendricks suggests that perhaps the associations between these nutrients and cervical cancer are early rather than late, citing a study that found an association between low vitamin B12 levels and persistent HPV infection (9). This study reported no association between folate and HPV persistence, however, and the same researchers also failed to find an association between either folate or vitamin B12 and HPV persistence among a smaller cohort of Hispanic women (6). Furthermore, if smoking- or oral-contraceptive-related folate/vitamin B12 depletion does adversely affect HPV infection status, we might expect to see a more consistent relation between smoking/oral contraceptive use and HPV infection in the literature; in contrast, the majority of studies have reported null associations (reviewed in our paper (2)).

While we do have banked serum from women enrolled in this study, there is some evidence to suggest that serum B12 radioimmunoassays may give falsely low results in oral contraceptive users (10) and that folate can be more accurately measured in red blood cells than in serum.

REFERENCES


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In their recent Journal article, Charles et al. (1) examined the association between prostate cancer mortality and occupational exposure to magnetic fields and polychlorinated biphenyls. The authors took advantage of the availability of a high-quality data set from a well-described occupational cohort. Numerous studies describing results from analyses of the same data set (e.g., Savitz and Loomis (2), Savitz et al. (3)) have contributed significantly to the understanding of associations between occupational exposure to magnetic fields and mortality from various causes.

The authors of this study (1) carefully weighed its strengths and limitations. They failed, however, to discuss one of the most serious limitations of their analyses. The study examined prostate cancer mortality rather than incidence. Mortality from any type of cancer is affected by not only the incidence of the cancer (which ideally should be used for etiologic research) but also the survival of cases after diagnosis. The survival of cancer cases could depend on various factors, such as the stage of cancer at diagnosis, the type of treatment, and the presence of any comorbidity.

For prostate cancer, the distinction between incidence and mortality is especially important. As a result of relatively good survival, there is a large discrepancy between prostate cancer incidence and mortality rates. The basis of data from the Surveillance, Epidemiology, and End Results (SEER) program (4), during 1973–1988 (a period included in the Charles et al. study (1)), the annual age-adjusted prostate cancer mortality rates were, on average, only 29 percent of the corresponding annual age-adjusted prostate cancer incidence rates among White men (range, 24–35 percent) and 38 percent among Black men (range, 35–41 percent).

To illustrate the unreliability of mortality data as a substitute for incidence data, we can look at racial differences in incidence and mortality rates for prostate cancer in the United States. Based on SEER data (4), during 1973–1988, the annual age-adjusted incidence rates were, on average, 1.51-fold higher among Black men than among White men.
(range, 1.38–1.63). During the same period, the annual age-adjusted mortality rates were, on average, 1.99-fold higher among Black men than among White men (range, 1.82–2.15). The twofold increase in the death rate among Black men compared with White men is only partially explained by the higher incidence among Black men. On the basis of available evidence, it seems that the additional increase in the mortality rate among Black men is the result of their poorer survival because of a combination of later-stage diagnosis for Blacks and differences in treatment between Blacks and Whites (5, 6). Racial differences in stage at diagnosis and treatments are likely to stem from cultural and socioeconomic differences between the two ethnic groups (6, 7).

Similarly, men in typical high-magnetic-field-exposure occupations (e.g., linemen) could also systematically differ in many social, economic, and cultural ways from other, unexposed workers. If any of those characteristics is associated with survival, the observed difference in prostate cancer mortality between exposed and unexposed workers may not reflect real differences in prostate cancer incidence rates.

Although the study (1) was well designed and executed, and the results were clearly presented, the value and interpretation of the results are questionable. Because of the use of mortality data, these results provide no reliable support for a possible etiologic relation between magnetic field exposure and prostate cancer development. Interpretation of the results becomes even more problematic when we consider the lack of convincing laboratory evidence in support of a possible biologic basis for prostate cancer development. Despite the lack of consistent results from several epidemiologic studies, the interpretation of the results remains problematic when we consider the lack of convincing laboratory evidence in support of a possible etiologic relation between magnetic field exposure and prostate cancer incidence rates.

In his letter to the editor, Dr. Mezei (1) raises an important issue regarding a limitation of our study (2), which investigated risk factors for prostate cancer mortality rather than incidence. Although the distinction between cancer incidence and mortality is likely to be familiar to most readers of the Journal, we acknowledge that prostate cancer mortality is affected by various factors, including the ones cited by Dr. Mezei, and agree that a short description of the limitations of mortality data in our study would have been helpful to some readers.

However, we disagree with his assertion that “the value and interpretation of the results are questionable” (1, p. 929) because the study was based on mortality data. For differential survival to confound associations of prostate cancer with exposure to magnetic fields, substantial differences in prostate cancer survival would have to be associated with cumulative exposure. However, our analyses included only those workers employed by five large companies within a single industry. Large differences in culture and socioeconomic position are less likely to confound associations in such internal comparisons than in community-based studies that sample from the population at large. Moreover, access to medical care is likely to be relatively uniform within a cohort of workers from the same industry.

Undoubtedly, additional studies designed to control for biases from several sources would have to be conducted before it can be concluded that electromagnetic field exposure is an etiologic agent for prostate cancer development. Our study (2) makes an important contribution to the literature on prostate cancer mortality, and it adds another layer to the foundation of studies from which epidemiologists and laboratory scientists can build to further investigate whether a causal relation exists between exposure to electromagnetic fields and development of prostate cancer.

**REFERENCES**


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