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Invited Commentary: Electromagnetic Fields and Cancer in Railway Workers

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The ideal study of occupational exposure to electromagnetic fields and cancer risk would have a clear exposure source, historically stable exposures, and comparable groups of exposed and unexposed workers. Cohorts of railway workers have marked exposure contrasts and limited job changes and provide marginally adequate study sizes, but there have been important changes in their exposures over time, and the field frequency involved is unusual. The results of Minder and Pfluger's study (*Am J Epidemiol* 2001;153:825–35) add modest support for an association between electromagnetic field exposure and leukemia. However, given the large size and high quality of a number of previous studies of occupational electromagnetic field exposure and cancer, additional studies similar to past ones are unlikely to yield important new insights. *Am J Epidemiol* 2001;153:836–8.

brain neoplasms; electromagnetic fields; environmental monitoring; leukemia; occupational exposure

Epidemiologic research on the relation between occupational exposure to electromagnetic fields (EMFs) and risk of cancer (especially leukemia and brain cancer) has advanced considerably in the past 20 years. Starting with simple tabulations exploiting available mortality data (1) or cancer registry data (2) on electrical occupations, studies have evolved to include increasingly sophisticated approaches to exposure assessment, detailed consideration of confounding, large study sizes, and refined analytical methods. Tens of millions of dollars have been spent, most of it wisely, to improve upon previous study methods in an attempt to resolve the question of whether occupational exposure to EMFs constitutes a health hazard. Unfortunately, the barriers to reaching definitive conclusions transcend financial limitations or a lack of ingenuity among those of us who have addressed the issue. Neither money nor creativity can overcome the inherent limitation of insufficient sizes of the populations available for study or the challenge of assessing or reconstructing EMF exposures. The greatest source of ambivalence regarding continued pursuit of the hypothesized carcinogenic effects of EMFs continues to be the lack of experimental support and, some would argue, the lack of plausibility that such support will ever be found.

What would constitute the ideal opportunity for a study of occupational EMFs and cancer? This benchmark of unattainable perfection provides a referent for examining the current study by Minder and Pfluger (3), as well as other recent studies of railway workers (4–6), electric utility workers (7–11), and community populations (12, 13). In the ideal setting, there would be a single, well-defined source of EMFs, allowing simple calculations of exposure based on the geometry of the workplace and the worker's location. The workers would be physically stable in their jobs relative to that source, not leaving their work stations for extended periods during the workday. This work environment would be historically stable, with no innovation in technology or changes in the manner in which the work was done to alter exposure. Within a given industry, there would be other jobs that were identical in terms of training requirements, selection, and associated pay and prestige but free of elevated EMF exposure.

In such an ideal study, assignment to high- and low-exposure jobs should be as close to random as possible and should be stable throughout a worker's entire career. Other potentially carcinogenic exposures, occupational or nonoccupational, should be absent or equitably allocated across EMF exposure groups. There should be tens of thousands of exposed workers in order to examine the rare cancers of interest, and accurate cancer incidence data should be available. The exposure patterns under investigation should be sufficiently similar to those of other work settings and, ideally, similar to residential exposures for easy extrapolation of the results to other populations.

The job assignments, locations, and activities in the railway industry offer investigators a good opportunity for such study but not an ideal one. In this issue of the *Journal*, Minder and Pfluger (3) have demonstrated a marked contrast in estimated EMF exposures across major job groups for present-day work activity. In their study, line engineers had approximately double the magnetic field exposure of shunting line engineers, eight times the exposure of train attendants, and 26 times that of station masters. These estimates were based on magnetic field measurements made at different work locations for exposure incurred while performing specific tasks involving equipment currently in use. While decomposing occupational exposure into its compo-

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Abbreviation: EMF, electromagnetic field.

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nent parts by work task and location allows for flexibility in reconstructing historical exposure using different weights for the component parts, it poses the challenge of accurately assessing the amounts of time spent under those homogeneous exposure conditions and the exposures incurred in each. An alternative approach, one that has been widely employed in studies of electric utility workers (7, 8, 14), is to take measurements of a large number of randomly selected workers with the intention of capturing the actual exposures encountered by workers, even if the contributing factors are too complex to be fully identified. However, as long as the railway magnetic field environment is simple, with limited diversity in location and exposure within each site (in contrast to the electric utility industry), Minder and Pfluger's approach is preferable.

With regard to historical stability, it seems that there have been major changes over time in the Swiss railway industry, and those changes have undoubtedly been accompanied by dramatic changes in exposure for certain workers. To the extent that the exposure implications of those changes can be fully understood, such changes represent meaningful, strategically useful variability in exposure to be studied; to the extent that they cannot be captured, the changes will result in misclassification.

The size of Minder and Pfluger's railway workforce was large and quite sufficient for major cancers, but it was marginal for such rare cancers as leukemia and brain cancer. The opportunity to examine subtypes of leukemia, for example, or alternative indices or time periods of exposure would require studies larger than this one.

The rarity of job changes over the workers' careers is a clear strength of the Swiss railway study (3), though even in that setting some changes occurred. While quantitative assignments of exposure allow aggregation across jobs that differ in exposure, the simplicity of being able to compare job groups directly without the assumptions required for aggregation is advantageous. The nature of how the railway workers chose their jobs or were chosen for the different jobs was not addressed, so it is unclear whether there was selection that may have related to future risk of cancer. It appears that the workers were largely free of other potentially carcinogenic workplace exposures.

Perhaps the biggest drawback of the railway study is its uncertain applicability to other workplaces and the community more generally. The frequency of the magnetic fields encountered (16⅔ Hz) is distinctly different from that of the power-frequency magnetic fields most commonly encountered in homes and workplaces in the United States (60 Hz) and much of the rest of the world (50 Hz). While all of these frequencies fall within the extremely low frequency range and may have common biophysical properties, uncertainty about mechanisms of biologic interaction and possible human health consequences introduce uncertainty into the extrapolation.

The key substantive contribution of Minder and Pfluger's paper is contained in their table 3 (3, p. 829), which calculates risk by job category. In comparison with station masters, line engineers (highest exposure) experienced increased risk of leukemia, shunting yard engineers had increased risks of leukemia and brain tumors, and train attendants had increased risk of brain tumors. Such a pattern across job groups and outcomes suggests that EMFs alone could not be responsible. The results are imprecise, as one would expect given the small number of cases. Across the four job categories and two types of cancers (defining eight cells), four cells had five or fewer cases, and only two had 10 or more cases. Many potentially interesting questions concerning the effect of exposure duration, calendar time of employment as an indicator of exposure, and temporal relations between exposure and disease could not be addressed. The additional analyses that employed indices of exposure in categories (table 4) or exposure as a continuous measure (table 5) verified that higher exposures are associated with higher risks of leukemia, but they entailed such severe imprecision for brain cancer as to be of dubious value for this outcome. The motivation for creating an index of exposure is to integrate experience across diverse jobs held by a worker over his or her career and to try to discern whether the pattern observed across jobs is fully explained by exposure to the agent of interest. Since the analysis was limited to the workers' longest-held job and the numbers were too small to distinguish a "job effect" from an "exposure effect," the benefits of using the exposure index are modest. Combining the uncertainty regarding exposures incurred within jobs due to variation in equipment and changes in job tasks with the uncertainty of historical extrapolation of exposure in those jobs renders the exposure indices susceptible to substantial misclassification.

Minder and Pfluger's study (3) adds markedly to the limited literature on leukemia and brain cancer among railway workers, which is most pertinent to exposure to 16⅔-Hz EMFs. The study size was largely consistent with previous evaluations, and the methods of exposure assessment and analysis were also equal to or better than those of previous studies. The study helps to address random error by providing an additional set of data on railway workers: Given how much of a problem random error is in this literature, this is no small contribution. There continues to be sporadic support in the literature for increased risks of leukemia and brain tumors among railway workers with elevated exposure to 16⅔-Hz magnetic fields. If one were asked to compare the prior and posterior estimates of the probability that such exposures cause leukemia and brain cancer, Minder and Pfluger's study would raise the probability of a modest association for both types of cancer (more so for leukemia than for brain cancer).

For elucidating the possible roles of occupational EMFs in neurologic disease (15), cardiovascular disease (16), and breast cancer (17), which have received only limited empirical evaluation, the strategies that have been pursued to examine leukemia and brain cancer are certain to add important information, regardless of the pattern of findings. However, what do we do now to advance our understanding of EMFs as a potential cause of leukemia and brain cancer? Each new study of tens of thousands of workers with millions of person-years of observation and detailed exposure measurements will add to the insights obtained from studies that came before. Each will add a new dot on the graph or a new line in the summary table. The weight of evidence will move up or down modestly as a function of study quality and findings; but the number, size, and quality of such studies required to shift our overall assessment from “a possible modest association” to confirmation or refutation makes them unaffordable and inefficient. For each new study that is contemplated, we should ask whether the magnitude of the shift in evidence we are capable of achieving will alter our interpretation of the total body of evidence with regard to causal inferences, policy decisions, or planning for future research.

One approach would be to suspend further epidemiologic studies of the relation of EMFs to leukemia and brain cancer. It is difficult to argue with the proposition that conducting more studies of the same type, even those of the high quality of Minder and Pfluger’s (3), will have limited benefit. The possibility of obtaining more substantial insight from further epidemiologic research would be markedly enhanced by new discoveries about the hypothesized exposure-disease association. Most obviously, a replicable laboratory finding addressing the etiologic pathway of interest would allow for manipulation of exposure patterns to identify the forms of human exposure most likely to increase risk of cancer. Research would then be needed to determine how to capture those forms of exposure in epidemiologic studies, and previously examined or new populations of workers could be evaluated. Such a breakthrough in the laboratory would both inspire and guide a new generation of epidemiologic inquiry. Closely related to this elusive goal is the hope of identifying an intermediate endpoint for epidemiologic study as a suitable substitute for these rare cancers—one that has a continuous rather than a dichotomous outcome and that responds over short periods of time rather than long periods. Some investigators are pursuing alterations in melatonin levels as a candidate for such an intermediate endpoint (18, 19), which allows for tight linkage of monitored exposure and health outcome.

I have argued elsewhere that the ability to function without an understanding of biologic mechanisms is a strength of epidemiology over other disciplines (20). In the absence of information on biologic mechanisms, no other scientific approach is available for assessing the potential for human health harm. In the absence of experimental evidence linking EMFs to cancer, epidemiologists have proceeded appropriately. However, making optimal use of sophisticated epidemiologic approaches has not provided a satisfactory resolution of the issue with regard to causal inference or policy. Without some unique circumstances offering vast numbers of unambiguously exposed workers, some new integrative indicator of exposure, or a surrogate endpoint allowing new study designs, it seems that “black box” epidemiology has exhausted its potential for contributing to a resolution of this question.

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