BOOK REVIEWS

Advances for Epidemiology

Biomarkers and Occupational Health. Progress and Perspectives. MORTIMER L. MENDELSOHN, JOHN P. PEETERS, and MARY JANET NORMANDY, Eds. Joseph Henry Press (National Academy Press), Washington, DC, 1995. x, 335 pp., illus. $54.95. Based on a workshop, Santa Fe, NM, April 1994.

What happens to the buzzwords of yesteryear, such as "biomarkers" and "molecular epidemiology"? Happily, sometimes they mature to represent productive avenues of research that give new life to older disciplines. In this case the "older discipline" is epidemiology.

"Biomarkers" have been known for some time simply as biological measurements. They can be used in epidemiology as indicators of exposure (for example, a blood level of a toxicant or a DNA adduct level in a tissue), susceptibility (for example, the level of expression of an activating or detoxifying enzyme for a particular toxicant), or early effect (for example, the cellular incidence of specific DNA mutations in target tissues). Use of biomarkers can help break open the black box that lies between human exposure and diagnosable cases of illness or death in conventional epidemiology.

Biomarkers also hold the promise of providing useful information for monitoring and prevention efforts before sufficient death certificates accumulate for traditional studies. In a spectacular demonstration in this volume, Brandt-Rauf *et al.* report that 15 (83%) of 18 workers exposed to vinyl chloride who developed angiosarcomas expressed a specific G-to-A transition at the second base of codon 13 of the *c-Ki-ras-2* gene. Examining exposed and unexposed workers without angiosarcoma, they found that 49% of 45 exposed workers but none of 28 control workers had detectable p21 protein with the relevant mutation in their serum. The frequency of this occurrence was strongly associated with the numbers of years of exposure to vinyl chloride.

This book is a clear indicator of a maturing field. It resulted from a conference held to consider applications of the still-emerging technology for assessing and monitoring the hazards to former and current workers who contributed to the Department of Energy's extensive nuclear projects during the Cold War. The book of course includes good papers on biomarkers of radiation dose (by Straume and Lucas, Gray *et al.*, and Kelsey *et al.*), but it also has sophisticated discussions of the implications of relevant pharmacokinetics for the noninvasive monitoring of concentrations of volatile chemicals in exhaled air (Thomas, formerly Fiserova-Bergerova) and the development of an important genetic marker of susceptibility for the immune hypersensitivity reaction that causes chronic beryllium disease (by Saltini and Rossman), among other topics.

The consideration of applications here is a great deal more than technological boosterism. There are extensive contributions on practical ethical and legal issues (by Rothestein, by Rom, and by American Civil Liberties Union attorney Maltby), no fewer than four papers with "validation" in the title (by Perera, Rothman *et al.*, Rabkin and Rothman, and Straume and Lucas), and useful estimates of the costs of different genetic assays (by Albertini). Mendelsohn in an excellent paper early in the volume gives expanded data from his technical *tour de force* in finding a strong linear relationship between radiation dose and the incidence of glycophorin variants in the red cells of atomic bomb survivors, based on grouped data from samples collected over 40 years after exposure. Then he analyzes the difficulties of usefully applying current techniques to workers exposed to ionizing radiation at the levels experienced by the great majority of current and former Department of Energy workers (including temporal factors, sensitivity, and specificity). He recommends careful further development, with analysis of possible benefits and costs of specific applications, before a widespread measurement program is undertaken.

Promising as current biomarker techniques seem for epidemiology and medical monitoring, the future holds at least two possibilities for new biomarker technology that could transform cancer epidemiology. First, the capability to sequence the genes that are part of the molecular pathological pathway for tumors in individual people could provide the basis for a whole new categorization of disease outcomes with likely etiologic significance. Instead of just counting tumors by anatomical site and histological type, epidemiologists may be able to make use of the numbers of tumors with DNA changes associated with particular etiologic agents in particular genes. For example, radiation tends to cause a larger proportion of deletion mutations than most other mutagenic agents. Some future radiation-cancer epidemiological study might benefit by counting separately tumors at a particular site that have deletion-type mutations in specific genes (such as p53, or *ras*) on common cancer pathways. Such information may eventually be available for epidemiologists to draw upon if it proves of significance for prognosis or therapy and therefore begins to be generated in the course of normal medical practice.

An even more revolutionary possibility will be realized when technology is developed to measure the cellular frequency of known types of mutations along known cancer pathways in otherwise normal tissues obtained from autopsies or (in special circumstances) biopsies or from samples of normally exfoliated cells from particular tissues (such as bladder epithelium). Instead of waiting for members of a cohort of several thousand workers to develop cancer decades after the casual exposure and counting one case (or non-case) for each death, we could hope to find that the frequency of particular p53 or other relevant mutations in cells of this or that tissue is elevated in workers with this or that current or immediate past exposure. This would change the unit of analysis from the whole person to the individual cells in different tissues. Autopsies on 30 people with well-characterized exposures could well yield more useful dose-response information than conventional long-term cohort studies of groups hundreds of times as large.

This is a field that bears watching by a wider audience than those in the immediately concerned technical specialities.

Dale Hattis
Center for Technology, Environment and Development, George Perkins Marsh Institute, Clark University, Worcester, MA 01610, USA

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A Global Campaign

The War Against Hepatitis B. A History of the International Task Force on Hepatitis B Immunization. WILLIAM A. MURASKIN. University of Pennsylvania Press, Philadelphia, 1995. iv, 248 pp., illus. $29.95 or £28.50.

Hepatitis B infection is a major cause of chronic cirrhosis and primary liver cancer. Accounting for an estimated million deaths worldwide annually, hepatitis B virus is one of the most important carcinogens, second only to tobacco. For many countries in Asia and sub-Saharan Africa chronic carrier rates