Book Reviews

Monitoring the Effects of Therapeutic Agents

Epidemiological Evaluation of Drugs. Proceedings of a symposium, Milan, May 1977. F. COLOMBO, S. SHAPIRO, D. SLONE, and G. TOGNONI, Eds. Elsevier/North-Holland, New York, 1977. x, 334 pp., illus. $21.95. Clinical Pharmacology and Drug Epidemiology, 1.

The protection of the public from the unanticipated consequences of drugs is a challenging undertaking; there are a myriad of therapeutic agents in use, many with substantial variation in the way they are used, and the range of possible effects associated with the use of a particular agent can be broad. This book therefore raises issues of concern. The papers are essentially of two types: those that review recent findings on the relation of particular agents to specific diseases and those that consider various strategies for monitoring the effects of drugs. Although some new data are presented, the substantive papers are generally concise, evaluative summaries of recent findings on the adverse effects of specific agents. Some papers deal also with the efficacy of specific treatments. The review papers are linked to the more methodological papers by their discussions of the strengths and weaknesses of the designs used to evaluate the agent under review. The methodological papers in turn are linked to the substantive papers by the use of examples of strategies that have succeeded or failed in identifying certain associations. The result is a remarkably well-integrated series of papers with little redundancy.

The possible adverse effects of therapeutic agents range from acute to chronic, from immediate to long-term, from common to rare. This myriad of effects implies the need for different approaches to monitoring the adverse effects of drugs. Associations with rare diseases are most efficiently approached through case-control studies. Associations with relatively common conditions can be examined in prospective studies, provided data sets are developed in anticipation of the eventual need for a prospective investigation. Techniques for the surveillance of drugs include spontaneous reporting by physicians, case-control studies, multipurpose data systems, and specially mounted ad hoc studies; each has a role in the evaluation of drugs, and each is discussed from different perspectives in this book. At the conclusion of the book one is aware of the need for two data sets that can be linked: one containing information on drug use, perhaps obtained through pharmacy records, and one containing information on incidents of disease. This system, however, presents ethical problems to some and organizational and economic problems to most.

Throughout the book it is apparent that international collaboration has an essential role in the comprehensive and cautious evaluation of many marketed drugs. The necessity of such collaboration is obvious when either the use of the drug under investigation or the suspected adverse effect are rare; it may be only through the pooling of data that the suspected association can be examined. International collaboration also contributes an important dimension to the study of associations between drugs and less rare diseases. Investigation of a particular agent across several settings provides confirmation or refutation of an initial observation. Comparisons of findings across settings allow specification of the conditions under which the effects of the agent may differ. These conditions include not only differences in the patterns of use for the agent under investigation but differences in the use of other drugs, in patterns of disease, in environmental factors, and in genetic factors as well. Such comparisons contribute both to the elucidation of the pathogenetic mechanism of an agent and to the making of decisions about whether and how a drug is best used.

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Auditory Mechanisms

Psychophysics and Physiology of Hearing. Proceedings of a symposium, Keele, Staffordshire, England, Apr. 1977. E. F. EVANS and J. P. WILSON, Eds. Academic Press, New York, 1977. xx, 526 pp., illus. $27.35.

The symposium on research in hearing held at the University of Keele was the fourth in a series of such symposia and has resulted again in a valuable, well-organized collection of papers. The emphasis of the book is on mechanisms of frequency analysis, pitch perception, and temporal factors in hearing. Explanations for psychophysical phenomena are sought in physiological mechanisms of the auditory system.

Here it is only possible to point out a few of the many interesting conclusions presented in the book. In a section entitled Cochlear Mechanisms, Rhode reports evidence of tone-on-tone suppression effects at the level of the basilar membrane. Russell and Sellick investigate why tuning curves (showing the relation between threshold and frequency) for individual nerve fibers are sharper than mechanical tuning curves for the basilar membrane. They recorded intracellular potentials from individual inner hair cells and show that the tuning with frequency is as sharp as that of cochlear nerve fibers. They conclude that tuning occurs at the level of the hair cells and does not involve neural interaction.

Further important contributions related to frequency analysis and pitch perception are included in other sections of the volume. De Boer shows how several theories accounting for pattern recognition of low pitch are related. Evans in his paper and Bilsen and ten Kate in their comment on it point out that cells in the dorsal cochlear nucleus are able to resolve comb-filtered noise spectra over a wide range of noise levels, despite the saturation of cochlear nerve fiber discharge rates at higher noise levels. Evans suggests that neuronal lateral inhibition makes this resolution possible. In addition it is suggested that cochlear fibers can provide cues from the time structure of their discharge patterns even at high stimulus levels. Goldstein and Srulovicz show that the processing of interspike intervals can provide important information for the discrimination of single tones and also for the discrimination of tone components of a complex stimulus. Finally, Raatgever and Bilsen demonstrate that the low pitch perception produced by a delay in the arrival of a white noise stimulus to the two ears is a by-product of the mechanisms of