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

binaural hearing. They find that the dichotic pitch can be lateralized as a function of interaural delay and that the central patterns responsible for the perceived pitch also produce predictable binaural masking effects.

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Tree Physiology

The Structure, Biosynthesis, and Degradation of Wood. Proceedings of a meeting, Vancouver, B.C., Canada, Aug. 1976. FRANK A. LOEWUS and V. C. RUNECKLES, Eds. Plenum, New York, 1977. xii, 528 pp., illus. $49.50. Recent Advances in Phytochemistry, vol. 11.

The title of this important book is somewhat misleading because two of the 11 chapters have nothing whatsoever to do with wood and several others deal with wood only marginally. Some of the authors, for example Côté and Hillis, are familiar with the wood science literature, but others have obviously had no such adventures. Nevertheless there is a tremendous amount of useful information in the volume, and every serious wood scientist should have access to it.

Côté's chapter on wood ultrastructure provides an admirable overview that covers both normal and reaction wood. The chapter spans orders of resolution from light microscopy through scanning and transmission electron microscopy. One of Côté's theses is that the optical system used affects the nature of the structure observed. Unfortunately the resolution of the scanning electron microscope is incorrectly listed as 0.1 nanometer and that of the transmission electron microscope is somewhat underestimated. Côté views the cell wall as a continuous series of fibrils ranging in diameter from 1.7 to 150 nanometers or more. Côté suggests that the larger strands may be aggregates of the smaller ones or the smaller ones may be artifacts created from the larger ones by various mechanical means. This interesting idea should stimulate further debate. It is disturbing that only eight of the 52 references in Côté's chapter are from the present decade. At least in part, this is the result of inadequate funding of structural research.

Delmer reviews research on cellulose biosynthesis and provides some interesting information on the possible role of lipid intermediates in this process. Lamport's chapter on glycoproteins deals with such nonwoody matters as the evolution of eukaryotes. He also supports the interesting thesis that extensin and collagen have a common ancestry.

There are several excellent chapters on lignin and microbial degradation of cell walls. Gross has written an outstanding chapter on lignin biosynthesis that reiterates Freudenberg's view that the process is enzyme-initiated but differs from the synthesis of other biopolymers in that subsequent polymerization is nonenzymatic. Gross does discard the Freudenbergian notion that cinnamyl alcohols are synthesized in the cambium and transported to the xylem in the form of glucosides. It is now known that lignifying tissues possess all the enzymes and intermediates for complete lignification. There is also good coverage of the ligase-mediated activation of cinnamic acids with coenzyme A and the subsequent reduction of the substances to cinnamyl alcohols.

Hillis has provided a monumental and definitive chapter on secondary changes in wood. Mullick's chapter on wounds and pathogenic responses nicely complements the chapters on degradation. The book concludes with a chapter on the status and potential of chemicals derived from bark and wood. The production and editing of the book are first-rate. Overall the book is a valuable addition to the literature.

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Riverine Landscapes

The Fluvial System. STANLEY A. SCHUMM. Wiley-Interscience, New York, 1977. xx, 338 pp., illus. $22.

Erosion, transport, and deposition of sediment within river catchments concern a wide range of earth scientists and profoundly affect land management. Upland soil removal engages the attention of soil conservationists, hydraulic engineers deal with fluvial sediment transport and river channel morphology, and patterns of sediment deposition in riverine and coastal lowlands affect navigability, the habitability of valley floors, and the distribution of groundwater and minerals.

Schumm argues persuasively that fluvial geomorphology, sedimentology, and stratigraphy provide insights into each of these components of the river basin. He summarizes a great deal of recent geologic research to explain the relation between upland erosion, sediment transport, channel morphology, and deposition.

Schumm is successful in conveying a sense of the interdependence of upland, channel, and depositional environments and in describing the types of change that each component can undergo during various spans of time. He repeatedly makes the provocative suggestion that fluvial systems characteristically undergo rapid changes due not only to alterations in external controls (such as climate, tectonism, or land use) but to internal adjustments that can produce a complex sequence of changes resembling the effects of alterations in external controls. Traditional interpretations of rapid change in the geologic or instrumental record usually assume quite simple cause-and-effect relations. Schumm stresses than an understanding of and ability to predict the complexity of response to external change allows the earth scientist to anticipate and avoid land management problems and to interpret in a more productive fashion evidence for the occurrence of economically valuable geologic materials.

The book does not deal with the mechanics of geomorphic processes and therefore does not present a unifying physical theory of hillslope erosion, sediment transport, or river morphology. Instead the effects of various controlling agents and of internal adjustments are illustrated with field relations, laboratory experiments, and, in cases where data are not yet available, hypothetical reasoning. In some places these qualitative arguments are vague and open to question, though formalizing them would require a much larger book and would be impossible in some cases, given the current state of knowledge. They are thus indicative only of directions of change and have little value for quantitative prediction in a particular situation. They successfully demonstrate, however, the author's points that the forms and operation of fluvial landscapes can be correlated with and explained in terms of their major controlling factors and that changes in these controls, although generally thought to be slow, are significant for the management and exploitation of drainage basins.

The chapters on river channels and depositional environments constitute the best parts of the book, and they will be of greatest use in geological and engineering applications.

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