of paramount importance throughout the animal kingdom as well as in microorganisms, and one which appeared very early in the course of evolution. As animal cells became progressively more complex and specialized, they appear to have retained this basic regulatory system to control the rate of their activities. Thus in the course of evolution new types of specialized cells, rather than abandoning the cyclic AMP system for the regulation of their activity, developed a specialized sensitivity so that only very special types of chemical substances would be able to stimulate the synthesis of cyclic AMP in them and by this means trigger them into the performance of their specialized functions. Viewed within this framework, the natural occurrence and physiological effectiveness of cyclic AMP in a wide variety of dissimilar tissues become more readily comprehensible. It is just this diversity of processes in which cyclic AMP is involved that has puzzled many biologists and, ironically, delayed general acceptance of the importance of this molecule.

The book under review was written by members of the laboratory in which cyclic AMP was discovered. The book ranges over the entire field of cyclic nucleotide research and surveys most of the literature available at the time of writing. It contains particularly thorough accounts of the role of cyclic AMP in mediating the actions of catecholamines, in regulating carbohydrate and fat metabolism, and in controlling steroidogenesis. Other sections provide a discussion of the enzymes that catalyze the synthesis and destruction of cyclic AMP, a survey of the numerous hormones in whose actions cyclic AMP has been implicated, and a review of knowledge concerning the role of cyclic AMP in lower organisms. There are, in addition, three special chapters by individual authors: a fascinating historical account by Sutherland of the developments that led to the discovery of cyclic AMP; a description by Posternak of the chemical properties of the cyclic nucleotides and of laboratory methods for the preparation of cyclic AMP and various analogues; and a lucid chapter by Hardman on the biology of guanosine 3′,5′-monophosphate, a substance closely related to cyclic AMP and one that has attracted the attention of an increasing number of investigators within the past few years because of its possible importance as another intracellular regulatory agent.

Until about two years ago, one of the most important factors limiting research in this field was the enormous complexity of the methods available for assaying cyclic AMP. In an appendix, the authors describe the very complicated system used in their laboratory. The amount and brilliance of the research that has come from that laboratory are all the more impressive in view of the cumbersomeness of the methodology utilized until recently.

Scientists who have been working in this field will find the book useful as a well-written reference text. In addition, it should prove valuable as an introductory text to the many hundreds of scientists who have recently become interested in the cyclic nucleotides. One of the more valuable aspects of the book, for established as well as for new workers in the field, is the insight it provides into the thinking of a laboratory which has figured so prominently in this field since its genesis some 15 years ago.

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Pharmacological Tool

6-Hydroxydopamine and Catecholamine Neurons. A symposium, Bürgenstock, Switzerland, Oct. 1970. T. MALMFORS and H. THOENEN, Eds. North-Holland, Amsterdam, and Elsevier, New York, 1971. 368 pp., illus. $22.50.

At a Pharmacology Society meeting recently one of the contributors to this volume introduced his paper with the remark, "I second the nomination of 6-hydroxydopamine as the drug of the year." If anything, he understated the case, for it is possible that no compound since reserpine has proved so useful a tool in the investigation of catecholamine-containing neurons.

The drug (known as 6-OH-DA) produces what has been termed a "chemical sympathectomy" in vertebrates; but variations in experimental conditions and species have resulted in confusion and contradictions in the literature about its effects. This book is a collection of papers presented at a closed symposium sponsored by F. Hoffmann-La Roche and Company for the purpose of clarifying the mechanism or mechanisms of action and organizing current knowledge of this research tool for publication. The editors wisely selected a multidisciplinary group of contributors to integrate the morphological, biochemical, and pharmacological aspects of the tribulations of catecholamine neurons subjected to 6-OH-DA.

The mechanism of action of 6-OH-DA is dependent upon relatively selective uptake into catecholamine neurons, depletion of amine, incorporation of the drug into granular synaptic vesicles, and, after higher doses, degenerative changes due to formation of toxic oxidation products in the neuronal cytoplasm. Peripheral adrenergic neurons are affected in a dose-dependent manner, their terminal axons (varicosities) appearing most susceptible and the cell bodies most resistant.

The drug produces either of two conditions, which are distinguishable only by electron microscopy during the first few days after dosing: (i) changes compatible with early degeneration, even in the cell body, with prompt reversion to normal appearance, or (ii) complete degeneration of the nerve terminals, which is reversible only if the cell body is not destroyed, and even then slowly.

Because 6-OH-DA does not cross the blood-brain barrier in the animals studied, it has been injected intraventricularly or intracisternally, and affects those norepinephrine- or dopamine-containing nerve cell bodies or terminals which receive the highest concentration of the drug. Intracerebral injection under stereotactic control is described by Ungerstedt as a precise and selective method of mapping catecholamine neuronal pathways in the brain. As in the peripheral neuron, the distinction between reversible and irreversible changes is difficult, and, as Bloom points out, even cell bodies which appear heavily damaged several weeks after injection may still be viable.

The book is divided into sections dealing respectively with (i) peripheral neurons, (ii) central neurons, (iii) effects on adrenergic function, and (iv) mechanism of action, and a fifth section containing papers which must have seemed inappropriate for inclusion in any of the other four. Several of the papers are abundantly illustrated with fluorescence or electron micrographs. The fluorescence micrographs are generally quite good; a few of the electron micrographs are technically imperfect (probably because they represent early work of the investigators—this reviewer pleads guilty to similar faults) or are of too low a magnification to permit easy interpretation. At the end of the

volume is an abbreviated version of the important points of discussion pertaining to each section, edited by the chairmen of the respective sessions (section 2, on central neurons, is far too brief), and finally a résumé of a few related papers published subsequent to the symposium.

Although both Malmfors and Thoenen speak English quite well, it is the native language of neither editor, and the book would have been improved by a careful reading to eliminate the frequent errors in spelling, style, and typesetting. These detract slightly from the readability but not at all from the general utility of the book, which will close gaps in the knowledge of even the best-informed specialist. For research workers who tamper casually with catecholamines it will prove more reliable and comprehensive than a telephone call to the nearest pharmacologist for the best recipe to extinguish adrenergic function. Both the methodology and the functional results pertaining to an important research tool are collected as well as possible in this volume, and the importance and breadth of the material included are greater than the title may imply.

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Antimalarial Agents

Chemotherapy and Drug Resistance in Malaria. W. PETERS. Academic Press, New York, 1970. xviii, 876 pp., illus. $39.50.

Studies carried out about a decade ago demonstrated conclusively that certain strains of *Plasmodium falciparum*, in parts of South America and in parts of Southeast Asia, were resistant to chloroquine and to other widely used synthetic antimalarial agents. These observations, reinforced by problems with drug-resistant malaria parasites subsequently encountered by American military personnel in Southeast Asia, shattered complacency with antimalarial drugs that had developed during the 1950's and contributed to a marked resurgence of investigative interest in malaria. The 1960's witnessed a rejuvenation of basic research on malaria and of intensive efforts aimed at the development of new antimalarial agents.

A rekindling of older investigative approaches together with the successful application of a variety of new experimental techniques yielded a wealth of new information about the effects, limitations, and mechanisms of action of, and about resistance to, antimalarial drugs. This book provides a timely and comprehensive summary and discussion of earlier and more recent data pertinent primarily to drug resistance. It is a valuable compendium of otherwise widely scattered information relating to the biology of malaria parasites; host-drug-parasite interactions; older and newer methods for assessing effects of antimalarial drugs in vivo or in vitro; experimental techniques for inducing drug resistance; results and implications of studies of malaria parasites of lower animals; results of studies of parasites that cause human malaria; the use of drug combinations in an effort to thwart the emergence of drug-resistant parasites; mechanisms of action of and of resistance to antimalarial drugs; entomological, immunological, and genetic aspects of drug resistance; and the impact of drug resistance on malaria control and eradication programs.

Those well versed in malaria will not have great difficulty spotting occasional arguable statements; overall, however, such instances will prove remarkably few in view of the immense amount of information considered. Coverage of different aspects of the subject is thorough, use of tables is extensive, and illustrations are numerous and excellent. Although references are not numbered, my count indicates that 1709 are cited.

This book is in essence a very detailed progress report that provides considerable insight into methodology and the state of our knowledge relating to drug resistance in malaria as it existed at the end of the 1960's. It attests both to the notable advances that have been made on multiple investigative fronts and to the substantial extent to which our knowledge remains incomplete despite these advances. Although research carried out during the 1960's provided a great deal of useful new information about antimalarial drugs and drug resistance, many fundamental questions remain only partially answered and many pressing needs remain largely unmet. We need, for example, deeper understanding of the mechanisms involved in resistance to antimalarial drugs, more information about the factors that influence the geographic spread of drug-resistant parasites, better means with which to combat drug-resistant parasites, and more adequate insight into how currently available means can best be utilized.

The resurgence of malaria research during the 1960's offers hope that much-needed additional progress will take place during the 1970's. A major question, however, is whether it will be possible to sustain during the 1970's the investigative momentum developed during the 1960's. Peters begins by noting that problems with malaria during wartime have often provided the stimuli for accelerated research in malaria. He concludes by pointing out that malaria is likely to remain a formidable public health problem for some time. Perhaps one might add as a footnote the hope that the cyclic ups and downs of malaria research coincident with the beginnings and endings of wars will at long last be blunted so that exigencies of war will not constitute a prerequisite for waging a sustained investigative assault on malaria during the 1970's.

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Biophysics

Membranes and Ion Transport. E. EDWARD BITTAR, Ed. Wiley-Interscience, New York, 1970–71. In 3 vols. Vol. 1, xvi, 484 pp., illus. $22. Vol. 2, xiv, 296 pp., illus. $15.25. Vol. 3, xiv, 382 pp., illus. $18.

Though this three-volume work, dedicated to the late Edward Conway, is written primarily for the novice, many a membranologist should find it highly informative and generally interesting. Considering the dynamic nature of the field and the voluminous literature on ions and membranes, the heroic task of selecting subject material and imposing a reasonably consistent viewpoint on 34 contributing authors has been well done. Many of the contributors approach their subjects by comparison of traditional findings and concepts with current information, rendering gently persuasive arguments for alterations of existing theory. Though this informational rather than overtly critical approach is inherently sound, the reluctance of a few authors to offer substantive critical comment appears excessive. The reader, particularly the novice, is not