

acute and subacute toxicity of the various types of antiCHE compounds is discussed by DuBois. The neurotoxicity of organophosphorus compounds (in poultry and man) is summarized by Davies. The chapter by Wills is a critical survey of the various types of pharmacological antagonists of the antiCHE agents and their modes of action. The review by Hobbiger on the activation of phosphorylated ACHE contains considerable information on the metabolism, toxicity, and therapeutic applications of PAM-2 and related compounds. The two chapters by Grob deal with (1) antiCHE intoxication in man and its treatment, and (2) the usefulness of antiCHE agents in the treatment of myasthenia gravis. Leopold and Krishna have compiled a review on the local use of antiCHE agents in ocular therapy.

There is considerable overlapping of subject material from one chapter to another. For example, the therapeutic applications of PAM-2 in organophosphorus (antiCHE) poisoning in man is covered in Chapters 21 and 22 in different degrees of detail. Sometimes the same references are repeated and listed. A certain degree of overlapping is both useful and unavoidable because the subject material in different chapters is closely related. Different or contrary opinions on the same subject are evaluated critically by the different authors. For example, the role of ACH in axonal conduction of nerve impulse is discussed by three contributors—Nachmansohn, Hebb, and Koelle. The three authors arrive at different conclusions and, thus, a certain degree of overlapping has served a useful purpose.

This volume should be of great interest not only to research pharmacologists and to research workers in related disciplines, but also to entomologists and environmental health scientists. However, it should be pointed out that, although the book deals mainly with antiCHE compounds, many of which are used as insecticides, very little space is allotted to a discussion of the insect's nervous system, the role of ACH-CHE-CHAC system in the insects, and the mechanism of insecticidal action. Only one chapter (16) is allotted for the action of antiCHE compounds on insects. Brief discussions on this subject are included in the chapters by Hebb (3) and Karczmar (5 and 17).

The literature seems to be thoroughly covered through 1961. The price of the volume may not be too high to pay for this convenience.

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Diuretics. Chemistry and Pharmacology. By GEORGE DE-STEVENSON. Volume I of **Medicinal Chemistry, a Series of Monographs**. Edited by GEORGE DESTEVENSON. xiii + 186 pp. Academic Press, Inc., New York, N. Y. 1963. \$7.00.

This book is the first of a series of monographs on medicinal chemistry and, since it was written by the editor of the series, presumably should set the pattern for the rest of the volumes.

The first chapter sums up in eleven pages the "general physiological and pharmacological considerations" for renal function and the pharmacological evaluation of diuretics. After this are presented separate chapters on the various classes of diuretics—xanthines, triazines, organomercurials, sulfonamides, thiazides, aldosterone antagonists, and a miscellaneous group. The book concludes with an eleven-page chapter on the therapeutic use of diuretics in the treatment of hypertension.

A major problem in reviewing (and writing) a book of this type is to decide what constitutes proper coverage of the topics discussed, and even what topics to include. This reviewer feels that medicinal chemistry should be defined as the design and synthesis of potential therapeutic agents. In order to be effective, the practitioner must be thoroughly familiar with the methods of evaluation and the mode of action (if known) of his agents, and the limitations of the clinically useful compounds, as well as with the structure-activity relationships and methods of synthesis. In general, the success of a medicinal chemistry project in developing a lead depends on how keenly the biological aspects are brought to bear on the synthetic aspects of the problem. The more precisely a new compound can be evaluated, the more useful will it be in influencing the choice of new compounds to be prepared.

The present volume is an excellent, comprehensive, and up-to-date treatment of the synthesis and structure-function aspects of the various types of diuretic agents. However, the detailed discussion of the known or probable reasons for these structure-function relations seems to be rare. Thus on page 116, there is a table of a dozen thiazides which shows a thousandfold potency difference between chlorothiazide and cyclopentthiazide. Certainly, some of the factors contributing to this, such as a comparison of protein binding, distribution, relative sites of action in the tubule, blood levels, and rates of excretion are known for at least some of these compounds. Such considerations might explain some of these potency differences and indicate which areas might be more profitably explored.

The section on renal physiology, according to the preface, was "written in a relatively uncomplicated and concise manner so that all those not well versed in the field could readily understand the dynamics of renal function." Unfortunately, the level of understanding that could be gained by reading this section would also be uncomplicated. The type of testing described in the section on pharmacological evaluation does not reflect the methods used by a modern reasonably sophisticated renal laboratory. Surely, today no one would consider that much is known about the character of the activity of a diuretic until the results of several types of renal clearances obtained in several different physiological states are available. Only clearance studies reveal the effect of the agent on tubular electrolyte transport and filtration rate, and thus indicate those drugs with useful natriuretic properties.

The section on the use of diuretics in hypertension also seems to be written in a relatively uncomplicated manner. There is no clear agreement, contrary to the statement on page 161, that thiazides lower blood pressure as a direct consequence of their diuretic and natriuretic activity. The hypotensive activity of the salt-retaining thiazide diazoxide as well as other data at least suggest a direct hypotensive effect. For instance, changes in peripheral resistance independent of changes in extracellular fluid volume have been proposed as a major factor in the hypotensive effect of the thiazides. Also in the discussion of the clinical utility of the thiazides as diuretics, their potassium losing properties are mentioned, but today medicinal chemists should also be concerned with their uric acid retention properties and possible diabetogenic liability.

The present book is a valuable contribution to the literature, and has met very well the author's goal of "surveying the field in its entirety, with particular emphasis on the chemistry of diuretically active compounds and their structure-activity relationships." If the coming volumes in this series are up to the standards set by this one, then indeed the series "will act as a catalyst for further developments" as hoped by the author in his preface.

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International Pharmaceutical Abstracts. Volume 1. Edited by D. E. FRANCKE. 20.2 × 26.6 cm. Published by the American Society of Hospital Pharmacists, 2215 Constitution Ave., N. W., Washington, D. C. 20037. 1964. \$15.00 (individual subscription).

This new abstract journal will appear biweekly, and offer abstract articles from all major and standard journals, 450 journals so far, in the following areas: biopharmaceutics, physical pharmacy, pharmaceutical technology, pharmaceutical chemistry, pharmacology, investigational drugs, drug evaluations, adverse drug reactions, drug laws and regulations, and the history, ethics, sociology, and literature of drugs. There will be at least 6000 abstracts annually, each abstract averaging 200 words, except for shorter abstracts of legal, trade, and professional articles.

While there will be some overlapping with *Chemical Abstracts*, the collection of abstracts of medicinal and pharmaceutical interest under one cover, and the promised rapid appearance of abstracts after publication of the journal articles should persuade any scientist in the field, and all professional pharmacists, to read this welcome new organ.

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