**Progress in Drug Research.** Vol. 5. E. JUCKER, Ed. Birkhäuser Verlag, Basel, Switzerland, 1963. 654 pp. Swiss Francs 124.

The fifth volume of this series contains three chapters: The effects of structural alteration on the anti-inflammatory properties of hydrocortisone by L. H. Sarett, A. Patchett, and S. Steelman (142 pages, 371 ref.); Analgesia and addiction by L. B. Mellet and L. A. Woods (111 pages, 199 ref.); and Phenothiazines and azaphenothiazines as therapeutic agents (E. Schenker and H. Herbst, in German, 357 pages, 6,800 ref.). An author and title index for Vol. 1–5 is appended. Each chapter is distinguished by completeness, by progressing from descriptive chemical and biological data to searching inquiries into the mechanisms of action on a molecular level, and by reviewing clinical applications in the light of structural modifications. All three chapters feature well written historical introductions which lead us from chance observations by mystery-story-like pathways to the decisive discoveries. Many of these facts have not been presented accurately before.

The monumental chapter on phenothiazines is the most descriptive of the three but will remain the factual reference work in this field for a long time. The review of potent analgetics has gathered much material from earlier review articles and books but goes well beyond them in its interpretation of theories of analgesia and addiction. The chapter on hydrocortisone and its many anti-inflammatory congeners fills a much-needed gap in steroid compilations. Most reviews of steroid chemistry and pharmacology have covered so many areas of this diversified field that details had to be treated by reference rather than by discussion. The original grouping for even a justification for congeners of hydrocortisone makes interesting reading. The Merck scientists offer a critical and probing survey of all pertinent facts and ideas both on the "how" and the "why" of steroid anti-inflammatory activity. Although the interpretation of steroid receptors remains speculative, the authors have penetrated as deeply as facts, reasoning, and scientific hoping will permit at present. These pages should be read as a model as to what contemporary knowledge can do with the concepts of bioreceptors.

It is not too much to say that this is one of the best volumes of the series. If future volumes are to be measured by its standards, they will offer the most penetrating reviews of medicinal science available today.

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**Grundlagen der Arzneimittelforschung und der synthetischen Arzneimittel.** By JAKOB BÜCHI. Birkhäuser Verlag, Basel and Stuttgart, 1963. 744 pp. Swiss Francs 96.

Although adequate texts and reference books covering all phases of the chemistry of drugs have been available in English, no such compendium has appeared in German in recent years. Professor Büchi, who has just been celebrated in European medicinal journals as an outstanding modern pharmaceutical chemist on that continent, has returned this compliment by writing a large, learned, yet very readable book on the fundamentals of the science of drugs. The second part of the title, involving synthetic drugs, points to the older preoccupation of pharmaceutical chemical research and education: the application of organic chemistry to the preparation of medicinal agents. But Prof. Büchi has taken a significant step forward. He recognizes that the synthesis and manufacture of drugs are activities of organic chemistry and make such compounds available for study and therapy, but do not contribute in any way to the understanding of drug action; nor do they help in the conception of new structures of potential medicinal interest. The present book deviates, therefore, from previous texts on drug chemistry: it does not report or discuss synthetic methods by which drugs are prepared but is concerned with the discovery of drugs, with their properties and their mode of action. The organically trained pharmaceutical chemist may pout over this lack of synthetic or degradative chemical information, but he should realize that to be a medicinal chemist, one has to lean towards more than pure organic chemistry.

This pioneering step in designing the book is counterbalanced by the inclusion of 43 pages on physical pharmacy (pp. 239–247, 289–324) which has only a peripheral value to drug design. On the positive side, the book is the first of its kind to devote a full chapter on drug metabolism and the impact of biochemical alteration on activity. To the medicinal chemist this area is of ever-growing interest, and a compact survey of this work is highly welcome. The nonpharmacologist will be glad to find an excellent simple chapter on biological methods of evaluation of drugs, and a carefully conceived short section on clinical trials reflecting the latest regulations and difficulties imposed on such experiments.

Professor Büchi is an authority on the relation of physical properties and pharmacological activity, and the chapter devoted to this topic (120 pp.) goes well beyond the scope of similar reviews. So does the chapter (60 pp.) on the mechanism of drug action which describes what we know of biological, cellular, and biochemical receptor sites, modes of drug-receptor interactions, and the moderate amount of enzyme chemistry a medicinal chemist ought to know.

The main portions of the book deal with structure–activity relationships and their application to the design of new medicinal agents. Metabolite antagonism is treated somewhat as a stepchild, but the author has succeeded in stressing other aspects suggestive of new and needed researches, even in therapeutic fields in which the cause of the disorder is not understood. The novel subdivision of the book and the extensive literature coverage make for refreshing and useful reading.

American medicinal chemists will perhaps wish that the book were written in English. But even if that wish could be accommodated by translation, the text would have to be adjusted extensively to American usage, especially in drug nomenclature. Most drugs are given European registered trade names in the present volume rather than generic names. Many new drugs of the last five years in rapidly moving fields (antineoplastic agents, psychotherapeutic drugs, etc.) are not mentioned. Nevertheless, the new organization of the material, and the enthusiastic persuasion of the ethically satisfying mission of medicinal science should make every medicinal chemist want to read this book.

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**Entstehung, Wachstum und Chemotherapie maligner Tumoren.** By DIETRICH SCHMÄHL, University of Bonn. Editio Cantor, Aulendorf i. Württemberg, Germany. 209 pp. 17 × 24 cm., 62 figures. DM 28.

This small book attempts to give an all-too brief survey of cancerogenesis and all types of therapies of malignancies. It is addressed to the medical student and practitioner; the oncological scientist will not derive too much benefit from the over-all sketchy presentation of data. Perhaps the best portions of the book deal with animal experimentation, and with a review of exogenous carcinogens from radiation through every type of chemical to tars from tobacco smoke and smog. There is a good chapter on malignant growth phases, and on metastasis. The chapter on the radiological therapy of cancer is reasonably adequate but the section on the huge modern effort in tumor chemotherapy is not. It reflects the gap between experimental and clinical therapy as seen by a clinical pathologist. Perhaps such conservatism is as it should be, but it does not inspire confidence in research in a field where clinical failure is still the current end of the road.

There is an author index but no subject index.

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**Metabolic Inhibitors. A Comprehensive Treatise.** Vol. 1. Edited by R. M. HOCHSTER and J. H. QUASTEL. Academic Press, Inc., New York, N. Y. xx + 669 pp. $26.00 (subscription price for each of two projected volumes $22.00).

The inhibition of metabolic pathways, enzymes, and especially of metabolites is one of the few defendable approaches to drug

design open to the medicinal chemist. Those who still argue that even this working hypothesis is tenuous will change their minds after contemplating the massive evidence presented in the first of the two volumes of this treatise. The subtitle "comprehensive" is no exaggeration. The careful preparation of each chapter, the measured clear judgement accorded to each fact stressing specificity and multiple actions, and the extensive and up-to-date literature coverage justify this designation. Smaller earlier monographs on biological and metabolic antagonism will be superseded by these books.

It has been suggested that many medical sciences should be grouped together in a department of metabolite antagonism. The titles of the chapters of the present book support such a view. They are (with authors): amino acid analogues (W. Shive and C. G. Skinner); polypeptides and proteins as inhibitors (E. J. Modest, G. L. Foley, and S. Farber); hexose and pentose analogues (R. M. Hochster); fatty acids and their analogues (P. G. Scholefield); phospholipids (J. B. Davenport); purine analogues (G. H. Hitchings and G. B. Elion); pyrimidine analogues (R. W. Brockman and E. P. Anderson); nucleic acids and nucleoproteins (K. A. O. Ellem and J. S. Colter); inhibition of amino acid decarboxylases (W. G. Clark); inhibitors, antagonists and inactivators in the etiology of diabetes mellitus in man (A. Mirsky); antagonists to fat-soluble (J. Green) and water-soluble (D. W. Wooley) vitamins; sulfonamides and folic acid antagonists (T. H. Jukes and H. P. Broquist); thyroxine analogues (S. B. Barker); inhibitors of steroid actions and cholesterol and steroid biosynthesis (R. I. Dorfman). The list of illustrious experts writing about their long-time major fields of interest is assurance of high standards. The only unsatisfactory chapter which could be termed sketchy is the last one; it barely touches upon the feverish activity in its field. Lest someone be disappointed by the absence of some major classes of anti-drugs, the titles of the chapters should be read with care. For example, only structural analogues of thyroxine are discussed in Barker's chapter while the bulk of antithyroid agents has not been mentioned.

The aim of this book is to present truly biochemically proven antagonists, and not just over-all structural analogues, some statements of Woolley's notwithstanding. A biochemically based definition of antagonists has long been needed; it should not discourage blue-sky dreaming about structural analogies but should require substantiation of these assumptions by enzymatic or biological experimentation. Every organic chemist who toys with the potential biological effects of structural analogs of metabolites should study this volume. So should biochemists and medical scientists, as well as microbiologists, nutritionists, botanists and others who wish to read about methodology, theory, and available results in this sprawling field of work.

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**Medicinal Chemistry.** Vol. VI. Edited by ERNEST E. CAMPAIGNE AND WALTER H. HARTUNG. Prepared under the auspices of the Division of Medicinal Chemistry of the American Chemical Society. John Wiley and Sons, Inc., New York and London. 1963. x + 356 pp. 22.5 × 24.5 cm. $10.00.

In the sixth volume of this series, whose first volume appeared in 1951, the tradition of unequalled completeness in a relatively restricted field of therapeutic agents is continued in three chapters: non-barbiturate hypnotics (245 pp., 723 references) (K. W. Wheeler); spinal cord depressants derived from polyols (43 pp., 77 ref.) (E. J. Pribyl); and X-ray contrast media (58 pp., 207 ref.) (J. O. Hoppe). Each chapter contains a brief historical review, a statement of the chemistry and physical properties of the compounds involved, a section on structure-activity relationships, and surveys of the pharmacology and uses of the materials. The bulk of the chapters consists of tables listing *every* compound with the respective activity, from the early 1900's to 1960. It may be assumed that no compound listed under pertinent reference terms in almost any journal, has been overlooked. On the other hand, this indiscriminate completeness has been achieved at the expense of selectivity. No one can do much with a statement in the literature that a compound is a "slight hypnotic," without any additional data, and it is doubtful whether such compounds should have been included. Also, one would wish for the more abundant use of generic instead of trademarked names in a scientific publication beamed at chemists and biologists. But these are minor faults. The great advantage of this series is the hope that further literature searches for the compounds under discussion should not be necessary.

With the appearance of other excellent reviews, though not as complete, one may wonder whether the editors of the various series could not coordinate their efforts to avoid substantial duplication. Also, these other series of review volumes on medicinal chemistry have whetted the reader's taste for a more enjoyable style that goes beyond the strict account of established facts. Editors of future volumes may well consider such a recommendation to their authors.

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# *Additions and Corrections*

1961, Volume 3

**J. D. P. Graham and G. W. L. James.**

Page 490. In Table I, the legend for compound $L_{21}$ should read R′ = R″ = $CH_2$=$CHCH_2$.

1963, Volume 6

**G. Brooke Hoey, Robert D. Rands, George DeLaMater, Douglas W. Chapman, and Philip E. Wiegert:** Synthesis of Derivatives of Isophthalamic Acid as X-Ray Contrast Agents.

Page 24. In column 2, line 1, for isothalamic read iothalamic.

**Alfred Burger, Robert T. Standridge, and E. J. Ariens:** Cyclopropyl and Cyclobutyl Analogs of Phenyl-Substituted Medicinal Agents.

Page 221. In the abstract, line 2, for N-methylsaccinimide read N-methylsuccinimide. In column 2, line 11, for presumable read presumably.

Page 224. In column 2, line 66, for ethyl actetate read ethyl cyanoacetate.

Page 225. In column 2, line 50, for ether read acetone; in line 68 for azine read azo compound.

**L. Goldman and J. W. Marsico:** Synthesis and Reactions of 3′-Amino-3′-deoxyribosides of 6-Chloropurine.

Page 414. The structural formulas in column 1 should be included in footnote 27.

Page 417. The structural formulas at the top of column 1 should be included in footnote 40 on page 416.