antiviral agents have displayed useful therapeutic properties in man holds out hope that the chemical treatment of viral disease is entirely feasible. If the mechanism of action is interference with nucleic acid synthesis, selectively acting agents must be developed which will not interfere with normal cell metabolism when administered systemically. Furthermore, such drugs must be capable of inhibiting virus production *after* the infection has started, since a mere prophylactic action is at best impractical from the therapeutic standpoint. The agent need not be virucidal but should check viral production until the body has been able to develop sufficient antibodies to produce an immunological response. A highly effective virucidal agent would prevent the development of immunity and leave the body defenseless against subsequent viral infections by the same virus, since resistance and cross resistance develop quite readily with many types of antiviral drugs. It is, therefore, desirable to allow a relatively high antibody titer to develop, thereby assuring the body of permanent or semipermanent protection against future infections by the same virus.

The synergistic effect of anti-inflammatory agents in enhancing the action of antiviral agents in animal is worthy of note, even though cortisone will exacerbate viral infections.

The chapter on "The Vinca Alkaloids" by Neuss, *et al.*, is a well-balanced treatise on this new group of antileukemic agents from the standpoint of covering the chemistry, pharmacology, antitumor, antiviral and clinical properties of this interesting class of alkaloids. Both vinblastine and vincristine have received extensive clinical trial, the former being active in chorioepithelioma, Hodgkin's disease, and other lymphomas and the latter inducing complete remissions in childhood leukemias. Although the two drugs are structurally related, there is no cross-resistance. Especially gratifying is the fact that laboratory testing methods were able to forecast the clinical therapeutic potential of these agents. What one misses in this chapter are follow-up studies regarding the duration of these remissions, particularly in the area of acute childhood leukemia. Presumably, such data were not yet available at the time this paper was written. This may also hold true in regard to the incidence of clinical side effects which these compounds may elicit during chronic administration.

The largest chapter in the book is devoted to "Cell Culture and Cancer Chemotherapy" by Foley and Epstein. It is a highly authoritative treatise which covers the details of experimental procedures of working with cell and organ cultures and clearly points out the potential scope of this technique for the study of drugs on a molecular level. It deals with such important topics as drug resistance, the nutritional and metabolic requirements for cellular growth which unfortunately appear to be quite similar for the normal mammalian and neoplastic cells, membrane permeability and its alteration by drugs, the role of RNA in cellular differentiation, the possible mechanism of action of Actinomycin in the therapy of lymphoma and Wilms tumor, the comparative merits of the mammalian cell culture, and other *in vitro* systems in drug evaluation and the measurement of drug sensitivity.

The experimental evidence presented by the authors supports their contention that there is a remarkably good correlation between drug-induced inhibitory activity in mammalian cell assays and experimental antitumor activity.

The technique of organ culture would appear to be a highly effective tool for determining the mechanism of action of many diverse drugs, their inherent toxicological properties, and their propensity for inducing teratological effects. One must agree with the authors that this valuable assay tool has certainly not received the attention it should in the study of the mechanism of drug action and drug toxicology.

The authors conclude that the mammalian cell assays satisfy the criteria required of a useful screening procedure in the search for potential antitumor agents.

In his chapter on "Immunoreactions in Antiparasitic Therapy," Goble makes a strong plea for the concept of the "eternal triangle" of the "drug–host–invader complex." The chemotherapy of infections, as the author rightly points out, must be regarded in terms of a triangular relationship between drug, parasite, and host, with the dependence of the ultimate therapeutic effect on the defense mechanism provided by the body. Thus, drugs are viewed as "adjuncts" to meet the emergency before the body is able to take over.

With this triad of a dynamic relationship, the author then proceeds with the discussion of the separate effects of each component: the action of the drug on the host and *vice versa*, the various effects of the chemotherapeutic agents on parasites and of the parasites on the drug, and the interaction of the host and parasite. With regard to protozoan infections, the following factors are considered: (a) species and age of animal in relation to drug efficacy, (b) therapeutic regimen in relation to drug efficacy and development of immunity, (c) the ability of a chemotherapeutic agent to induce antigenic variations, (d) chemotherapeutic agents as tools in the study of immunity, (e) the interference of certain steroids with the body's defense systems, (f) conditions which will avoid or suppress immunoreactions and thereby favor the development of drug resistance, (g) the mechanism of host cooperation in chemotherapeutic cure (the reticuloendothelial system must remain intact for the immunological response to occur), and (h) the prevention of the immunological response by too premature and too massive chemoprophylaxis. These principles are discussed further in relation to the treatment of malaria, trypanosomiasis, and coccidiosis.

The chapter on "Drug Synergism in Antineoplastic Chemotherapy" by Venditti and Goldin strikes, of course, at the heart of cancer chemotherapy. The goals of multiple drug therapy are: (a) the lowering of toxicity, (b) the increase in efficacy and survival time, and (c) the prevention of drug resistance.

The various obstacles which the host presents to successful chemotherapy are discussed, such as the physiological barriers to the penetration of the drug to the target organ, the physiologic disposition (premature binding of drug at sites other than the target organ), biotransformation of the drug (some drugs will accelerate their own metabolism on chronic administration), and the too rapid excretion of the drug. All of these factors indicate the need for the addition of chemical agents which can overcome the disadvantages of single drug therapy. Several examples of such drug synergism are described by the authors including internal structural changes of an active drug by incorporating "transporting"moieties, such as phenylalanine, in the nitrogen mustards which increase survival time of mice with Sarcoma 37 several fold.

The discussion of the biochemical basis for drug synergism and drug resistance forms an integral part of this chapter. The authors conclude with the statement that thus far no dramatically active drug combination has been discovered in cancer chemotherapy.

The most challenging chapter from the standpoint of presenting new vistas in chemotherapy is by Kaplan and Friedkin on "New Concepts of the Use of Inhibitors in Chemotherapy." This chapter should be of particular interest to the medicinal chemist working in the field of chemotherapeutics.

The concept of "feedback" or end-product inhibition is a rather fascinating departure from the classical antimetabolite approach. The administration of the terminal metabolite in an enzymatic reaction sequence may produce a powerful block to the first enzyme reaction in the sequence. In the same vein, the administration of an inhibitor of the biotransformation of the terminal metabolite would produce an accumulation of this metabolite and, thereby, initiate a negative feedback and blockade of the first reaction step in the enzymatic reaction sequence.

In the light of this concept of "allosteric inhibition," the authors discuss many of the important enzyme systems in the body which would lend themselves to such an approach and would form the basis for rational drug design.

Another biochemical concept suggested by the authors is the "redirecting" of cellular metabolic pathways by genetic control. Such new pathways might be more susceptible to chemotherapy.

The interference with messenger RNA synthesis by Actinomycin D is due to the specific formation of an unusual Actinomycin–DNA complex which results in the inhibition of RNA synthesis. The authors feel that such a mechanism may have "implications of vast importance, since the synthesis of enzymes is the dynamic expression of genetic information residing in RNA and DNA."

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The Chemistry of the Antibiotics used in Medicine. By R. M. Evans, D.Sc., D.I.C., F.R.I.C., Glaxo Research Limited, Greenford, Middlesex. Pergamon Press Inc., 44-01 21st St., Long Island City, N. Y. 1965. x + 226 pp. 13 × 19.5 cm. 25s.

While it is proper that many volumes and monographs should be concerned with the medical uses, biological activities, and methods of production of the antibiotics, it is pleasant to find this small volume which concerns itself with the *chemistry* of these substances. As its title indicates, it encompasses primarily those antibiotics which have found use in clinical medicine. But by discussing

chemically and biologically related compounds and analogs, the author manages, as well, to present a fairly inclusive survey of the chemistry of most of the antibiotic types. He has included enough of the historical development of this important new field of chemotherapy and sufficient of its challenging aspects to furnish the student with an appreciation of what is still a dynamic research field.

The detailed chemistry is presented comprehensively, although summarily, as must be the case when dealing with such complicated work in a short space. Bibliographic references, however, are given which can lead the reader to the original publications. The author has made use of the biogenetic derivation of the antibiotics to classify them for structural chemistry discussion. This is a wise choice since it permits much chemical, as well as chemotherapeutic, correlation.

With regard to the purpose for which it was designed, an introduction for chemistry students to a broad area of natural product research, this attractive, typographically impeccable volume should find a ready acceptance.

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Optical Rotatory Power of Steroids. By J. JACQUES, H. KAGAN and G. OURISSON. General Editorship, S. ALLARD. Prefaced by W. KLYNE. Pergamon Press Inc., 44-01 21st St., Long Island City, N. Y. 1965. 1046 pp. 21 × 27 cm. $60.00.

This new edition of the well-known "Pouvoir Rotatoire" needs no introduction to steroid chemists. Many hours of searching the literature can be saved by the use of this extremely useful volume. The book supplies in very well-organized tabular form melting points, specific rotations, and literature references for more than 21,000 steroids described prior to 1961. This is 13,000 more than were listed in the 1956 edition. Although the volume lists only compounds described prior to 1961, references are included up to the end of 1963. The present tables relist all the compounds covered in the first edition, taking note of any revisions in structure or physical constants. A most welcome difference from the 1956 tables is the addition of the melting points of all the listed compounds. Lack of space has pursuaded the editors not to list rotatory dispersion data but to designate those references where ORD data may be found. The nomenclature used, which is fully dealt with in the introduction (French and English) follows closely the recommendations of the subcommittee on steroid nomenclature of IUPAC. In those instances where IUPAC recommendations are not yet available, the editors have provided very thoroughly considered extensions of the existing nomenclature. An alphabetical index employs trivial names wherever possible, in addition to the systematic names, a helpful device, particularly with complex structures. The critical attitude, which the compilers of this volume have taken, is apparent from correspondence which this reviewer has had with Mme. Allard regarding discrepancies of rotational values reported for the same compound by different authors, which, in some cases, had to be settled by repreparation of the compounds and repetition of the measurements.

The usefulness of this book to workers in the steroid field can hardly be exaggerated. This is in no small measure due to the very well-organized bibliography totaling 6300 references. It is a volume that should be found not only on library shelves but also in the laboratory where steroid research is carried out. This recommendation is made in full realization of the relatively high price of the volume, which, incidentally, is well bound to withstand the extensive usage that such a book is liable to be subjected to.

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BOOKS RECEIVED, *February 1966*

M. R. F. ASHWORTH. "Titrimetric Organic Analysis." Part II. "Indirect Methods." Interscience Publishers, John Wiley and Sons, Inc., 605 Third Ave., New York, N. Y. 1965. 1023 pp. $32.50.

S. COFFEY, Editor. "Rodd's Chemistry of Carbon Compounds." 2nd Edition, Volume I, Part D. "Dihydric Alcohols, Their Oxidation Products and Derivatives." American Elsevier Publishing Co., Inc., 52 Vanderbilt Ave., New York, N. Y. 1965. 418 pp. $24.00.

T. L. COTTRELL. "Dynamic Aspects of Molecular Energy States." John Wiley and Sons, Inc., 605 Third Ave., New York, N. Y. 1965. 83 pp. $2.25.

WILLIAM G. DAUBEN, Editor. "Organic Syntheses. An Annual Publication of Satisfactory Methods for the Preparation of Organic Chemicals." Volume 45. John Wiley and Sons, Inc., 605 Third Ave., New York, N. Y. 1965. 118 pp. $5.25.

J. R. S. FINCHAM. "Genetic Complementation." W. A. Benjamin, Inc., 1 Park Ave., New York, N. Y. 1966. 143 pp. $8.75.

M. F. JAYLE. "Analyse des Stéroïdes Hormonaux." Tome III. "Spectres Infrarouges, Région 1300-450 cm^{-1}." Masson et Cie, 120 Boulevard Saint-Germain, Paris 6, France. 1965. 240 pp. 70 F.

V. KONDRATYEV. Translated from the Russian by G. YANKOVSKY. "The Structure of Atoms and Molecules." Dover Publications, 180 Varick St., New York, N. Y. 1965. 530 pp. $2.50.

J. A. KUCK, Editor. Translated by KURT GINGOLD. "Methods in Microanalysis." Volume II. "Wet Combustion and Catalytic Methods in Microanalysis." Gordon and Breach Science Publishers, 150 Fifth Ave., New York, N. Y. 1965. 412 pp. $21.00.

L. R. MCCREIGHT, H. W. RAUCH, SR., and W. H. SUTTON. "Ceramic and Graphite Fibers and Whiskers. A Survey of the Technology." Academic Press Inc., 111 Fifth Ave., New York, N. Y. 1965. 395 pp. $10.00.

BEAT MEYER, Editor. "Elemental Sulfur. Chemistry and Physics." Interscience Publishers, John Wiley and Sons, Inc., 605 Third Ave., New York, N. Y. 1965. 390 pp. $15.00.

R. KENT MURMANN, R. T. M. FRASER, and JOHN BAUMAN, Editorial Committee. "Mechanisms of Inorganic Reactions. Summer Symposium of the Division of Inorganic Chemistry of the American Chemical Society at the University of Kansas, Lawrence Kansas, June 21-24, 1964." JACOB KLEINBERG, Symposium Chairman. Advances in Chemistry Series, No. 49. American Chemical Society, Special Issues Sales, 1155 Sixteenth St., N.W., Washington, D. C. 1965. 266 pp. $8.00.

W. J. ORVILLE-THOMAS. "The Structure of Small Molecules." Monograph 1. American Elsevier Publishing Co., Inc., 52 Vanderbilt Ave., New York, N. Y. 1966. 189 pp. $9.50.

GERALD SCOTT. "Atmospheric Oxidation and Antioxidants." American Elsevier Publishing Co., Inc. 52 Vanderbilt Ave., New York, N. Y. 1965. 528 pp. $26.00.

R. H. TREDGOLD. "Space Charge Conduction in Solids." American Elsevier Publishing Co., Inc., 52 Vanderbilt Ave , New York, N. Y. 1966. 143 pp. $10.00.