

Book Reviews

New Trends in Nuclear Neurology And Psychiatry. Edited by D. C. Costa, G. F. Morgan, and N. A. Lassen. John Libbey & Co. Ltd., London, England. 1993. xii + 180 pp. 17 × 24 cm. ISBN 0-86196-401-2. \$36.00.

The synthesis of radiopharmaceuticals and their role in the complementary imaging technologies of positron emission tomography (PET) and single photon emission tomography (SPET) has fostered a productive synergy between nuclear medicine physicians and neurologists. This current monograph captures the highlights of a 1992 Annual Congress of the European Association of Nuclear Medicine convened in Funchal, Madeira. Divided into five main sections and nine chapters, the volume covers many aspects of the topic from historical background to clinical applications. Its contributions are comprehensive, and many contain a number of instructive color plate PET and SPET images. Each chapter is well referenced, several containing literature citations as recent as 1992, and a substantial subject index is included in the back of the volume. This text successfully chronicles the collaborative spirit of the meeting and would be useful to radiochemists, neurologists and psychiatrists. Future meetings of this kind would be well served by similar volumes.

Crist N. Filer

*E. I. DuPont de Nemours
NEN Research Products
Boston, Massachusetts 02118*

Perspectives in Medicinal Chemistry. Edited by Bernard Testa, Emilio Kyburz, Walter Fuhrer, and Rudolf Giger. VHCA, Basel and VCH Weinheim, Germany. 1993. xii + 644 pp. 17 × 24 cm. ISBN 1-56081-252-4. \$150.00.

This book comprises the written version of 39 of the 42 invited lectures delivered at the XIIth International Symposium on Medicinal Chemistry held in Basel in September 1992. The chapters are collected in a number of major subdivisions that include enzyme inhibitors, receptor ligands, drugs acting on nucleic acids and nucleic acid processing enzymes, ion channel ligands, drug design, drug targeting, and aspects of molecular toxicology.

For those of us who were fortunate enough to attend, the Symposium itself represented an exciting exchange of information, as the editors rightly point out in their preface. And by assembling these lectures into a very well edited, visually attractive volume, they have achieved their goal of more permanently recording these important perspectives of recent progress in medicinal chemistry. As one would expect, the bibliographic documentation of the individual chapters is appropriate to a lecture, rather than to the complete citation record found in a formal review article. The lecture format also gives rise to a very readable style, which is enhanced by double-spaced typography, numerous clear illustrations, and attractive color plates.

Given the broad scope of the symposium and of this volume, it is clearly not possible to provide a meaningful review of each of the contributions. It may be helpful, instead, to discuss a few representatives to give an idea of what awaits the reader.

A very stimulating and convincing discussion of the future of medicinal chemistry by D. J. Triggle introduces the work. One can quarrel only with his statement that "issues in the future of medicinal chemistry are not technical". Clearly, the precise determinants of molecular recognition, the central technical issue in medicinal chemistry, remain unsolved. We cannot be certain, for example, that a series of enzyme inhibitor analogs will bind to the target in an identical manner, as elegantly shown in the X-ray crystallography of serine protease inhibitors by D. Bonner and co-workers in another chapter. This type of uncertainty clouds every SAR and QSAR study and obscures the theoretical underpinnings of medicinal chemistry itself at this point in its development.

The important area of peptidomimetic design is ably discussed by R. Freidinger and a large team in a chapter on the application of general strategies for this problem to oxytocin antagonists. Approaches outlined in this study began with receptor-based screening both for peptide and nonpeptide ligands and culminated in lead optimization by conventional medicinal chemical techniques. A stimulating discussion by D. H. Rich on the implications of hydrophobic collapse for the design of peptidomimetics is also of relevance to this area, as is the treatment of induction or fixation of peptide conformation by K. Müller and associates.

An especially interesting discussion on the use of basic chemical reasoning to design new classes of enzyme inactivators rationally is presented by R. B. Silverman and colleagues with regard to monoamine oxidase inhibitors.

The comparatively low intensity of research in developed countries on the antiparasitic drug design that is so important to less developed nations has been sometimes criticized. Such studies are considered in two chapters of this volume. The synthesis of antimalarials by C. W. Jefford and co-workers begins with a natural product, artemisinin, identified through screening studies, and is extended by lead optimization techniques. By contrast, the design of new drugs for trypanosomiasis, a target for medicinal chemistry since the time of Paul Ehrlich, is undertaken using a structure-based approach by C. L. M. J. Verlinde and a consortium of collaborators. In this work, inhibitors were designed for the essential enzyme triose phosphate isomerase by an X-ray crystallographic analysis of the structure of ligands with this enzyme, followed by computational protocols.

There is a wealth of interesting, well-presented information in the other chapters, and numerous significant areas of medicinal chemistry are considered. The book will be enjoyed by medicinal chemists in a

variety of fields, and is a worthy candidate for personal and institutional libraries.

Manfred E. Wolff

*ImmunoPharmaceutics, Inc.
11011 Via Frontera
San Diego, California 92127*

Advances in Clinical Pharmacology. Drugs and the Lung. Edited by Clive P. Page and W. James Metzger. Raven Press, New York, 1994. xi + 607 pp. 16 × 24 cm. ISBN 0-7817-0135-X. \$125.00.

The current interest in the development of new drugs for pulmonary diseases has been spurred by recognition that these diseases are an increasing burden on health-care systems worldwide. The present volume divides efforts in this area into two sections: (1) standard therapeutic agents used in current practice and (2) novel agents and approaches that are just entering clinical practice or which are under preclinical investigation. Referencing is extensive throughout, making the book a valuable source for future referral for researchers in this area.

In the first section, each chapter discusses the strengths and weaknesses of a particular class of drugs and studies of their mechanisms of action and how this research indicates new directions. The main emphasis is on the place of each drug class in current clinical therapy, with, for example, β -agonists recommended for symptomatic relief, cholinergic antagonists for COPD, steroids for underlying inflammation, and mast cell stabilizers such as cromolyn for preventive therapy in exercise-induced asthma. Discussion of mechanistic aspects may help identify new directions for researchers,

as in the review on theophylline. In this regard, an excellent chapter on the role of immunosuppressive agents in asthma indicates considerable potential, although the authors could have given more precise information on the mechanism of cyclosporin A by mentioning cyclophilin, calcineurin, and interleukin-2. Overall, these chapters clearly delineate new opportunities with established therapy.

In the second section, prospects for the application of newer approaches to asthma therapy are reviewed. Many approaches offer to reduce over-reliance on standard therapies, as potassium channel openers may do for β -agonists by reducing bronchoconstriction without cardiovascular side effects and phosphodiesterase inhibitors may do for steroids by relieving underlying inflammation. In this regard, a chapter on leukotriene antagonists, which have demonstrated clinical efficacy in improving lung function and thus may reduce reliance on steroids, would have been welcome. The final chapters cover the important role of bradykinin, platelet-activating factor, tachykinins such as substance P, and cytokines in asthma. Also included is a chapter on adult respiratory distress syndrome, emphasizing that a combination approach may be necessary to control the overwhelming cascade of mediators responsible for this disease. An extensive subject index rounds out this particularly useful volume.

Overall, then, this book offers much to both clinical practitioners and researchers in the field and can be recommended to medicinal chemists working in the area as a valuable perspective on approaches to asthma therapy.

John A. Lowe III

*Central Research Division, Pfizer Inc.
Eastern Point Road Groton, Connecticut 06340*