

N-Nitroso Compounds: Occurrence and Biological Effects. Edited by H. BARTSCH, I. K. O'NEILL, M. CASTEGNARO, and M. OKADA. International Agency on Cancer, Health and Biomedical Information Programme, World Health Organization, 1211 Geneva 27, Switzerland, 1982. 753 pp. 17 × 24 cm. Price \$55.00 (Sw. Fr. 110).

This volume is comprised of the Proceedings of the 7th International Symposium on *N*-Nitroso Compounds held in Tokyo, September 1981. It includes 73 papers and draws from a wide range of scientific disciplines. Numerous experts present information on the formation, occurrence, and biological effects of *N*-nitroso compounds. Formation of *N*-nitroso compounds within the body is reported by several workers and is discussed in relation to the ingestion of various materials. Data are given on exposure to *N*-nitroso compounds in the general environment and from tobacco usage. New and important developments of methods and approaches are presented that could promote the understanding of basic mechanisms of carcinogenesis and which could also be readily applied to the detection and analysis of *N*-nitroso compounds or their precursors. Also presented are suggestions for possible future research on nitroso compounds. A possible drawback of the book is the limited coverage of nitrosoureas, an important group of compounds in cancer research and treatment.

The papers are short, easy to read, and most present considerable background information. Concise figures and tables are used when appropriate. There is an author index and a thorough subject index. A list of references is given at the end of each chapter to assist readers seeking additional information. This book, written entirely in English, contains an enormous amount of useful information and is recommended as a general reference book to anyone directly involved in work on *N*-nitroso compounds.

Reviewed by George A. Digenis
College of Pharmacy
University of Kentucky
Lexington, KY 40506

Side Effects of Drugs Annual 7. Edited by M. N. G. DUKES. Elsevier Biomedical Press B.V., P.O. Box 1527, 1000 BM Amsterdam, The Netherlands. 1983. 539 pp. 15 × 25 cm. Price \$70.25 (Dfl. 165.00).

Adverse reactions to therapeutic agents can result from many and diverse factors. Two reactions of major significance are the abnormal patient reaction to a drug and the development of unexpected toxicity when two or more drugs are administered together. *Side Effects of Drugs Annual*, which has been published annually in January since its inception in 1977, is designed to provide a critical evaluation of the literature and an up-to-date account of recent information relating to these drug reactions and interactions. In this regard, the current *Annual* covers reports published between July 1981 and June 1982. In general, only publications presenting new information are reviewed. The reports which are documented are based on material from the Excerpta Medica Database System, which screens approximately 4000 journals in nearly 20 languages.

Although each *Annual* edition can be used independently, they are best employed as supplements to the most recent edition of the parent reference, *Meyler's Side Effects of Drugs*, an encyclopedic resource that reviews all existing knowledge on adverse reactions. The greatest value of a regularly published supplement is that it permits a continuing discussion of problems associated with the use of drugs; the question of a drug-induced disease raised one year can be followed up in subsequent years as the evidence to confirm or deny its occurrence becomes available. In addition, the *Annual* is published at a time when scattered reports of an iatrogenic disease have appeared in the medical and pharmaceutical literature, but have not been the subject of critical editorials and other review articles.

Each year an introductory chapter entitled "Side Effects of Drugs Essay" has been published as a forum for the discussion of topics that

are of current interest. This year, the essay written by the Chief of the Product Related Disease Division of Canadian Department of Health and Welfare explores drug development and formulation in light of documented adverse reactions, suspected reactions, and mere accusations of the possibility of adverse drug reactions. As noted in the introduction to the essay, its writer has designed it to be controversial with the intention of exposing pitfalls and false conceptions. In addition, beginning in 1980 and continuing with the current edition, a valuable feature entitled "Special Reviews" printed in italic type and identified by the traditional prescription symbol has appeared. These reviews, found in many of the 51 chapters, are critical discussions of controversial areas or the publication of new findings that require revision of existing concepts. Many report the latest developments in issues of continuing concern such as interactions of lithium with other drugs, side effects of β -blockers given prophylactically after myocardial infarction, ketoconazole and the liver, and prediction of anthracycline cardiomyopathy. In addition to discussing the data, each review offers the reader information that is useful clinically in recognizing, evaluating, and managing the specific reaction.

The current edition continues the discussion of drugs used in nonorthodox medicine begun with the first *Side Effects of Drugs Annual*. This year, the authors review the reports of toxicity from herbal remedies as well as updating previous information on laetrite. The chapter on miscellaneous drugs includes a special review and update on surgical materials and other appliances.

The drugs discussed in *Side Effects of Drugs Annual* are classified according to their pharmacological properties or therapeutic use. They are accessed by consulting an index of drugs, an index of side effects, or an index of interactions. In addition, an index of synonyms enables the reader to identify specific drugs by their foreign brand name, investigational number, chemical name, or abbreviation. To facilitate rapid searching, the three major indices in the current *Annual* provide a complete listing of all references discussed in the previous three volumes of this series. The references in each chapter have been uniquely coded to identify those reports in which (i) the information presented is reviewed in some detail; (ii) the original citation refers only briefly to the information presented; (iii) the original citation presents detailed clinical evidence; and (iv) the original citation provides a brief clinical description. The code allows the reader to select the original source most useful in documenting a specific drug-induced side effect.

This is a superb reference which provides an invaluable source of information on adverse drug reactions reported in the literature during a 1-year period. Even though the *Annual* series are not intended to be used as comprehensive references sources, many of the chapters, and in particular the special reviews, make fascinating reading. The major drawback of this reference is its cost, but it should be a part of the collection of medical libraries, drug information centers, and hospital pharmacies, where it would be available to those who dispense as well as those who prescribe drugs.

Reviewed by Arthur I. Jackowitz
Director, Drug Information Center
West Virginia University
Morgantown, WV 26506

Adapted from a Book Review of *Side Effects of Drug Annual 6* by A. I. Jackowitz [Am. J. Pharm. Educ., 46, 317 (1982)], with permission.

Pathology of Tumours in Laboratory Animals, Volume III: Tumours of the Hamster. V. S. TURUSOV, Editor-in-Chief. International Agency for Cancer Research Scientific Publication No. 34. World Health Organization, 1211 Geneva 27, Switzerland. 1983. 461 pp. 18 × 24 cm. Price \$40.00 (Sw. Fr. 80).

This volume, sponsored by the World Health Organization, is the third in a series concerning tumors of laboratory rodents, *i.e.*, rat, mouse, and now hamster. The text contains a number of contributions from F. N. Ghadially, A. Cardesa, A. H. Handler, A. D. Kelman, A. Emminger, U.

Mohr, M. Greenblatt, G. Reznik, J. Althoff, F. C. Chesterman, H. Kirkman, R. L. Kempson, A. H. Dodge, L. D. Berman, E. Soto, I. S. Levenbook, O. L. Kolomyets, M. A. Nikolayeva, P. Straüli, J. Mettler, P. Pour, M. Rustia, H. E. Pogozianz, and O. I. Sokova.

The book was organized, as were the two previous volumes, on an organ approach, giving a description of the individual tumors of each organ based on histological tissue type. Included in each chapter is a discussion of (a) normal structure, (b) morphology and biology of tumors, (c) spontaneous tumors, (d) induced tumors, and (e) comparative aspects. Included in the normal structure section is a description of the organ's gross anatomy, histological type of tissue, and cell types. The morphology and biology of tumor portion relates the most prevalent types of tumors found in the organ in hamsters based on standard histological classifications of tumors.

The spontaneous tumor section deals with the incidence of a given tumor occurring naturally in various hamster colonies throughout the world. Limited factual records were obviously available to the authors to make their evaluation. The induced-tumor section discusses the ability to induce a specific type of tumor in hamsters with either chemicals, environmental agents, hormones, or radiation. In some cases, the number of successfully induced cancers is included for the reader's perusal.

The portion on comparative aspects relates the probability of a hamster cancer being a good laboratory model in cancer research. Comparisons were made where appropriate, relating similarities of hamster cancers to specific human cancers. Certain hamster tumor models related positively with hormone-, chemical-, or virus-induced cancers in the human.

Each organ chapter contains black and white photographs of exemplary tumors from hamsters demonstrating cell types, histology, and morphology points typical to that type of tumor, metastasis, viral inclusions, etc. A number of electron micrographs are included. Although expensive, the volume contains no color photographs, which could have enhanced the staining characteristic of the tissue.

The materials in each chapter are well referenced, although the citations are not of recent dates, *i.e.*, 1975–1983. Obviously, attempts were made to collect all available references on a given hamster tumor in this volume. The text is written in a concise, straightforward manner. It is complete and well organized in its treatment of the tumors. This particular volume would not interest most scientists in cancer research, since hamsters are not frequently utilized as tumor-bearing models. Nevertheless, the text is a good reference book and may interest some researchers in the future who wish to develop in hamsters a tumor model that mimics a specific tumor in humans.

Reviewed by Iris Hall,
Division of Medicinal Chemistry and
Natural Products
The University of North Carolina at
Chapel Hill
Chapel Hill, NC 27514

Manual of Laboratory Pharmacokinetics. By STEPHEN H. CURRY and ROBIN WHELPTON. John Wiley and Sons, One Wiley Drive, Somerset, NJ 08863. 1983. 189 pp. 15 × 23 cm. Price \$21.95.

In the preface, the authors state that their purpose in this book was to compile "experiments suitable for use in training laboratory workers in biopharmaceutics, drug metabolism, pharmacokinetics, and related topics." A review of this book must then address the relevance of this book to the pharmaceutical sciences and the degree to which it meets a perceived need.

The changing curricula of pharmacy schools, with an increasing emphasis on clinical relevance in contrast to basic science background of fundamentals, is of concern to many in education. Now with the growing need for pharmacokinetic input to dosage adjustment, the adequacy of the analytical chemistry component of the training becomes a concern. Some schools now seek to emphasize biopharmaceutical applications rather than compendial assays, but this trend is hampered by a scarcity of adequate texts and manuals, especially for instructors who are not personally involved in the biopharmaceutical and pharmacokinetic implications of drug and metabolite assay.

The use of this book as a text in an undergraduate sequence requires the cooperation of instructors in analytical chemistry, pharmacokinetics, and pharmacology. Any student who is exposed to the approach utilized here will be a better "relevant" pharmacist for the knowledge and experience obtained. First-year graduate students, not just in pharmaceuticals but also in medicinal chemistry, deserve an exposure to this or an equivalent text if they are not already receiving this knowledge through related biopharmaceutic assay courses and appropriate support pharmaceuticals and kinetics.

Each chapter of this book provides good theoretical treatment of the subject matter, has one or more laboratory experiments clearly illustrating the methodology but providing data for pharmacokinetic interpretation, and contains a set of references and reading material. Even more valuable, typical data from each experiment are considered in the Appendix to demonstrate how the data should be presented and interpreted.

A listing of the experiments provides a recognition of the diversity of techniques explored and reviewed. These include: (1) construction of tritium quench correction curve by the channels ratio technique, (2) absorption spectrum of potassium dichromate, (3) fluorescence of quinine, (4) thin-layer chromatography separation of mild analgesic anti-inflammatory drugs, (5) radioimmunoassay of digoxin, (6) measurement of pK_a values of sulfadimidine and its N-4 acetylated metabolite (including preparation), (7) relationship between pH and apparent partition coefficient, (8) tablet dissolution, (9) decomposition of indomethacin, (10) storage of nitroglycerin tablets, (11) Fisher-Parsons approach for the study of drug absorption *in vitro*, (12) determination of K and n for warfarin binding to bovine serum albumin, (13) displacement of warfarin from binding sites on serum proteins, (14) metabolism of drugs by enzymes of the liver microsomal fraction, (15) determination of K_m and V_{max} for butyral-cholinesterase using butyralthiocholine as the substrate, (16) excretion of imipramine and its metabolites by rats housed in metabolism cages (including preparation of imipramine N-oxide), (17) influence of urinary pH on salicylate excretion, (18) pharmacokinetics of sulfadimidine and N⁴-acetylsulfadimidine, (19) urinary clearance of these two and determination of acetylator status, (20) kinetics of ethanol elimination with simple measurement of drug effect, (21) measurement of sleeping times in mice, use of drug effect to assess drug metabolism, and pretreated animal differences, (22) turn-over of noradrenaline in rat hearts, and (23) pharmacokinetic models and problems.

An interested student could read this book and its model answers to learn a great deal regarding techniques and methodology without actually having any hands-on experience. Many students deserve the opportunity of studying this book for this reason. In addition many of the faculty of our schools would profit from a similar reading of this book to enhance their background in this area of pharmacy practice. It is sincerely hoped that this and similar books will provide the necessary unification of concepts of fundamental basic sciences with animal and human pharmacology and pharmacokinetics.

Reviewed by John H. Wood
School of Pharmacy
Medical College of Virginia Campus
Virginia Commonwealth University
Richmond, VA 23298