

REVIEW OF REVIEWS¹

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Reviews of significant pharmacological and toxicological studies are increasing at such a rate that it is hard to keep abreast of them. They vary greatly. Some are so specialized and infested with jargon that only experts in the field under review can follow them. Others are merely superficial outlines of what is new, prepared for the edification of professional health personnel. This review falls under the latter heading.

The number of scientific reviews is now so large that merely to index them annually requires two large, thick volumes, as are produced so well by computer technique by the Institute for Scientific Information, under the skilled direction of Eugene Garfield.

The annual *Advances in Pharmacology & Chemotherapy*, now in its fourteenth volume, is well edited by Garattini and his associates. The current volume contains reviews on the chemotherapy of schistosomiasis, on mechanisms of action of immunopotentiating agents, on 5-azacytidine as an anticancer drug, and on copper in mammalian reproduction.

New is *Advances in Behavioral Pharmacology*, edited by T. Thompson & P. B. Dews. The first issue has reviews of the behavioral pharmacology of tetrahydrocannabinols, ethanol self-administration, behavioral effects of amphetamine, and a brief history.

GENERAL

The basic properties and clinical applications of "transfer factor" are considered in a US Army Medical Research Symposium, edited by Ascher, Gottlieb & Kirkpa-

¹This review was completed July 1, 1977, for material available at that time. References are cited by author and are arranged alphabetically under *Literature Cited*. This review is dedicated to the memory of Elizabeth Wilson Leake (1896-1977) who has helped in this effort for many years.

trick. With 198 references, Blinks, Prendergast & Allen review photoproteins as biological calcium indicators. These bioluminescent reactions are ion specific and are inhibited by magnesium and barium. They are applied in microdetection of calcium uptake and release. Florey edits 18 reviews of analytical profiles of drugs, including L-dopa and methotrexate.

Freudenthal & Jones edit 30 reports on polynuclear aromatic hydrocarbons, covering their chemistry, metabolism, and carcinogenic properties. Karim edits 11 surveys of the physiological, pharmacological, and pathological aspects of prostaglandins, relating to nervous systems, respiratory, cardiovascular-renal, and alimentary systems, to eyes, and to blood coagulation, inflammation, tumors, and analogues.

The stability of 173 injectable medications after reconstitution is summarized by Kirschenbaum & Latiolais. Klayman & Copeland survey the design of antiradiation agents. Pellegrino, with 51 references, reviews the symbols and substance of prescribing and drug ingestion, from the two approaches that drugs should be easily available, or that they need strict control with no direct sale to the public.

MACROMOLECULES AND POLYPEPTIDES

Beck chairs a Ciba Foundation Symposium in honor of Sir Frank Young on polypeptide hormones from their molecular and cellular aspects, ranging from insulin biosynthesis, through biochemorphology or glycoprotein hormones, to growth-promoting actions of peptide hormones. Beers & Bassett edit an important symposium on membrane receptors for viruses, antigens, and antibodies, and polypeptide hormones. With 313 references, Bertaccini reviews active polypeptides of nonmammalian origin, dealing with kinins from insects, frogs, and reptiles.

Clark, Klee, Levitzki & Wolff edit a Dahlem conference on hormone and antihormone action at membrane receptors at target cells. Dewied offers a short survey of peptides in relation to behavior. A status report on kinins is given by Erdos.

With 56 references, Goldstein reviews endorphins, the opiate-like peptides in pituitary and brain. Potent and abundant are methionine-enkephalin and leucine-enkephalin, H-Tyr-Gly-Gly-Phe-Met-OH and H-Tyr-Gly-Gly-Phe-Leu-OH respectively. Snyder goes on to review the binding of morphine and its derivatives at specific receptor sites on brain and spinal cord cells, and the way enkephalins and endorphins may also act at these sites.

Kakkar & Thomas survey the chemistry and clinical use of heparin. Paoletti & Glueck edit nine reviews of various aspects of lipid pharmacology. Parsons edits 21 reviews of peptide hormones from characteristics of amino acids in a peptide hormone sequence to the regulation of protein synthesis by peptide hormones. Sedlacek & Seiler edit a Behring Institute Symposium on neuraminidase, commemorating Alfred Gottschalk (1894-1974), and considering the toxicity and immunogenicity effects of neuraminidase on glycoproteins, on the therapy of cancer, and on the induction of immunity. Wagener, Fontaine & Neumann review the pharmacology of essential phospholipids.

ABSORPTION, FATE, AND ELIMINATION OF DRUGS

Barza & Weinstein survey the pharmacokinetics of penicillins in humans. Berkowitz reviews the relation of pharmacokinetics to the pharmacological action of morphine, methadone, and naloxone. Bianchine & Shaw review the clinical pharmacokinetics of L-dopa in Parkinson's disease. Branch & Shand survey propranolol deposition in chronic liver disease. Crooks, O'Malley & Stevenson consider pharmacokinetics in the elderly.

Drug metabolism in thyroid disease is reviewed by Eichelbaum. Gottschalk & Merlis consider the pharmacokinetics of psychoactive drugs in relation to blood levels and clinical response. Hvidberg & Dam survey the clinical pharmacokinetics of anticonvulsants. Johnsson & Regardh review the clinical pharmacokinetics of β -adrenoreceptor blocking drugs. Klotz analyzes disease-induced changes in drug distribution volume. Drug interactions in relation to clinical pharmacokinetics are reviewed by Kristensen.

The regulation of drug entry into the central nervous system is surveyed by Rapoport in a review of the blood-brain barrier in physiology and medicine. Skelly, Arnold & Sicé review biological availability of drugs in relation to therapeutic equivalence. Stitzel, with 152 references, well reviews the biological fate of reserpine, detailing its absorption, distribution, binding to adrenergic tissue and to platelets, its oxidation, and microsomal metabolism. Testa & Jenner discuss the concept of region selectivity in drug metabolism.

With 34 references, Zathurecky proposes a standard terminology in biopharmaceutics and pharmacokinetics, offering 60 basic terms with translations into 17 languages, but not Arabic or Oriental.

CHEMOTHERAPY AND ANTIBIOTICS

The antibacterial and pharmacokinetic properties of tobramycin are reviewed by Brogden, Pinder, Sawyer, Speight & Avery. With 234 references, King compiles a full review on cephalosporins for the American Hospital Formulary service. Pfeiderer edits a large survey of the chemistry and biology of pteridines with much on folate chemotherapy. Mitsuhashi & Hashimoto edit 48 reviews on microbial drug resistance, covering from genetic and molecular factors with much on plasmids, to epidemiological aspects with much on *Pseudomonas aeruginosa*, to biochemical considerations dealing with lactamases, tiox acid, and fosfomycin.

DRUGS ACTING ON NERVES AND NERVOUS SYSTEMS

Bauer reports on the pharmacology of ipratropium bromide, a new anticholinergic agent. Birkmayer edits 30 reports dealing with the helpful effects of carbamazepine in epileptic seizures, drug-induced behavioral disorders, and pain. Bradley & Dhanwan edit 36 reviews on drugs and central synaptic transmission, going from dopa-

mine mechanisms through monoamine antagonists, to histamine as a central transmitter.

Costa & Greengard edit a series of discussions on the mechanism of action of benzodiazepines, including evidence for the involvement of γ -aminobutyric acid. At a Dahlem Conference on food intake, Garattini & Samanin survey anorectic drugs and brain neurotransmitters. Guth, Norris & Bobbin review the pharmacology of transmission in the peripheral auditory system, quoting 235 references, mostly relating to the olivocochlear bundle.

With 140 references, Omenn reviews current neurochemistry in regard to behavior, citing the various neurotransmitters, the neuromodulators such as cyclic AMP, the prostaglandins, peptides, and opiate receptors. Richens & Woodford survey anticonvulsants in relation to enzyme induction. With 105 references, Strichartz reviews molecular mechanisms of nerve block by local anesthetics, noting that specific models include membrane expansion, with surface cleavage, but that calcium ions are not involved.

ANALGESICS, NARCOTICS, AND DEPENDENCY

Bostrom, Larsson & Ljungstedt edit 18 reports with much discussion on the treatment and treatment evaluation of drug dependence. Bourne edits 31 articles comprising a treatment manual for acute drug abuse emergencies, running from differential diagnoses to special problems. In two volumes, Braude & Szara edit a series of reviews on all aspects of the pharmacology of marijuana or hemp, from chemistry to genetics and therapeutic potential. With 30 references, Castro & Malkus review radioimmunoassays of drugs of abuse in humans. Rapid methods are available for the important ones. Twelve more reviews on cannabis and health are edited by Graham.

The psychotropic effect of androgens is reviewed by Herrmann & Beach. Klawans edits a series of reviews on neuropharmacological problems involving schizophrenia, physostigmine, vitamin B-6, and increased intracranial pressure. Lader reviews the clinical pharmacology of anti-anxiety drugs. Lieber edits eight reviews on the metabolic aspects of alcoholism. Pradhan & Dutta offer a comprehensive examination of drug abuse, emphasizing diagnosis and management.

Anesthesia

In a review with 160 references, Duncan & Cullen suggest that anesthesia may be immunosuppressive. They survey effects of anesthetics on leucocytes, on phagocytosis, and on lymphocyte formation. Current anesthesia relies heavily on muscle-relaxing agents. Their action in relation to anesthesia is well reviewed in 15 essays edited by Katz. With 98 references, Kaufman reviews biophysical mechanisms of anesthesia, covering lipids, critical volume, protein conformational change, and microtubules. With 32 references, Trudell offers a unitary theory of anesthesia based on lateral phase separations in nerve membranes, involving lipid systems.

CARDIOVASCULAR-RENAL DRUGS

Davies & Reid edit 26 articles on the central effects of drugs on blood pressure regulation, ranging from experimental hypertension to the effects of clonidine on the baroreflex arc. Johnston discusses the effects of antihypertensive drugs on the renin-angiotensin system. Morgan & Mathison review the mechanism of action and biochemorphic relations of antiarrhythmic drugs. In a symposium on the regulation of blood pressure by the central nervous system, which was edited by Onesti, Fernandes & Kim, there was much on the angiotensin-renin system, and on antihypertensive agents such as clonidine and methyldopa.

Riddiough, with 208 references, reviews the prevention and management of adverse reactions to antihypertensive drugs, such as the diuretic thiazides, the sympatholytics, and the vasodilators. Tinker & Michenfelder, with 94 references, review the pharmacology, toxicology, and therapeutics of sodium nitroprusside, emphasizing its power to lower blood pressure, and its detoxification by rhodanase to thiocyanate.

TOXICOLOGY

Bond reviews the toxic reactions of glucocorticoids in humans. Burns & Lerner introduce 11 reports on phencyclidine toxicity and abuse. With 82 references, Chang & Katz note pathological effects on liver, kidney, and brain from chronic operating room exposure to halothane in concentrations of 10 to 500 ppm. Hahn discusses bone complications from anticonvulsants. Heimpel & Kern review drug-induced aplastic anemias.

Plaa & Priestly, with 527 references, review intrahepatic cholestasis induced by drugs and chemicals, including bile salts, steroids, phenothiazines, manganese, and erythromycin. These seem to cause intracanalicular alterations. Schardein offers a comprehensive survey of drugs as teratogens, going from analgesics to vitamins, and including evaluation of teratogenicity. Ziskind, Jones & Weill give a survey of silicosis and of dusts involved.

CLINICAL

An important symposium on trace elements in medicine was introduced by Burch & Sullivan. In this, Cotzias & colleagues discuss manganese-brain-dopamine interactions, and Becking reviews trace elements in relation to drug metabolism. With 26 references, Kern & Lipman offer a review of theophylline therapy. Pearlman reviews the pharmacology and clinical use of antihistaminics. The pharmacology of clonazepam and its usefulness in epilepsy are reviewed by Pinder, Brogden, Speight & Avery.

Prasad edits a volume on the significance of zinc and copper on our health, both from the standpoint of deficiencies and toxicity. Then, with Oberleas, he edits 21 reviews on trace elements in human health and disease, from aluminum to zinc.

Terry opens a symposium on the immunotherapy of malignant disease. Wagner gives a critical analysis of immunosuppressive agents in lupus nephritis. Whitley and associates survey adenine arabinoside therapy of herpes zoster.

MISCELLANEOUS

Ajodhia & Dix discuss drug-induced deafness and its treatment. Girard, Cattin & Cuevas review immunological mechanisms and diagnostic tests in allergic drug reactions. Gotz & Lauper, with 65 references, evaluate the steroid inhaler, beclomethasone, for bronchial asthma. Nimmo discusses drug effects on gastric emptying.

In a neat historical survey, Parascandola tells about drug therapy in Colonial and Revolutionary America. In reviewing drugs from the sea, Ruggieri uses 110 references to note drug sources from alginates to sponges, and finds that tetrodotoxin blocks axonal conduction in nerves. In two volumes, Samuelsson & Paoletti edit a large series of studies on prostaglandins and thromboxane in relation to receptors in various organ systems, and to inflammation.

With extensive references, Swanson & Cook, in considering drugs in relation to blood dyscrasias, list 807 drugs under their trade and public names. This is a useful compendium.

IN PROSPECT

With increasing specialization within the general scientific discipline of pharmacology and toxicology, there is increasing fragmentation of interest and publication. The special in-groups tend to develop their own jargon, their own techniques, and their own conventions. If pharmacology and toxicology are to continue as solid scientific disciplines, there will be increasing importance in promoting helpful reviews of the various special fields, so that all interested may be kept informed of what is going on. This is necessary for teachers.

Annual Review of Pharmacology and Toxicology well serves such a function. It is helpful to specialists in giving hints and clues regarding methods, concepts, and applications which have been found to be helpful to others. Such cross-fertilization among specialists in a broad discipline, such as pharmacology and toxicology, is essential if an overall advance in knowledge and its applications is to be maintained. Reviews can be what binds pharmacology and toxicology together.

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