

Cyclic Nucleotides II

Physiology and Pharmacology

Editors

J. W. Kobayashi and J. A. Nathanson



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Cyclic Nucleotides Part Ii Physiology And Pharmacology
Handbook Of Experimental Pharmacology Volume 58

Michael A. Bray, John Morley



Cyclic Nucleotides Part II Physiology And Pharmacology Handbook Of Experimental Pharmacology Volume 58 :

Cyclic Nucleotides P. D. Kebabian, M. D. Nathanson, 2012-12-06 Cyclic nucleotides are intimately involved in the consequences of either stimulation or blockade of receptors therefore an understanding of the biochemistry of cyclic nucleotides ought to be important for pharmacologists Pharmacology is a science that among other things investigates chemical compounds that affect the physiology of cells tissues and organs Frequently pharmacologists account for the effect of low concentrations of a drug upon a tissue by invoking the presence of a receptor upon the surface of the cell Traditional pharmacologists excelled at identifying and classifying the properties of receptors A J CLARK S monograph in the earlier series of the Handbook of Experimental Pharmacology CLARK 1937 summarized the mathematics underlying the traditional pharmacological approach towards receptors By its nature however classic pharmacology provided little useful information about the intracellular events occurring as a consequence of occupying a receptor for example ALQUIST 1948 identified the beta adrenoceptor but he did not provide any insight into how stimulation of the receptor produces tissue specific physiological responses The discovery of cyclic AMP by RALL and SUTHERLAND see RALL Vol I led to biochemical investigations of many different receptors including ALQUIST S beta adrenoceptor that share a cyclic nucleotide as a common factor in the biochemical mechanisms that translate the occupancy of receptors into physiological effects Ten years ago in the introduction to their monograph on cyclic nucleotides ROBISON et al 1971 commented on the rapid growth of interest in cyclic nucleotides over the preceding years

Biochemical Pharmacology of Blood and Bloodforming Organs James W. Fisher, 2012-12-06 The subject of this volume is to review chemical agents which affect blood and blood forming organs Significant advances made over the past several years in the purification of several hematopoietic growth factors such as erythropoietin and colony stimulating factor the availability of several other growth factors such as the interleukins which are important in regulating the production of red blood cells leukocytes megakaryocytes and platelets are discussed Numerous toxic chemical substances are being produced in our environment which people are exposed to daily causing a suppression of erythropoiesis myelopoiesis and megakaryocytopoiesis Attempts to evaluate both the therapeutic role of some of the newer growth factors such as erythropoietin in the anemia of end stage disease as well as colony stimulating factors in some hematopoietic abnormalities are also covered in this volume In addition numerous chemical factors in our environment which suppress major hematopoietic lineages stimulated by erythropoietin macrophage colony stimulating factor granulocyte colony stimulating factor interleukin 1 alpha 1 beta 2 3 4 5 6 and 7 are also included In addition chapters on the use of erythropoietin in the treatment of anemia of end stage renal disease can provide the practicing hematologist and nephrologist with updated information on the use of erythropoietin for this disease The book includes chapters on the fundamental control of hematopoiesis and other mechanisms of action of erythropoietin and finally an up to date overview of the chemotherapy of leukemia This book will prove useful to investigators in the fields of pharmacology physiology

nephrology urology hematology pathology endocrinology biochemistry and molecular and cell biology **Pharmacology of Intestinal Permeation II** ,2012-12-06 The intestine particularly the small bowel represents a large surface in the adult 2 human approximately 200 m through which the body is exposed to its environment A vigorous substrate exchange takes place across this large surface nutrients and xenobiotics are absorbed from the lumen into the bloodstream or the lymph and simultaneously the same types of substrate pass back into the lumen The luminal surface of the intestine is lined with a leaky epithelium thus the passage of the substrates in either direction proceeds via both transcellular and intercellular routes Simple and carrier mediated diffusion active transport pinocytosis phagocytosis and persorption are all involved in this passage across the intestinal wall The term intestinal permeation refers to the process of passage of various substances across the gut wall either from the lumen into the blood or lymph or in the opposite direction Permeability is the condition of the gut which governs the rate of this complex two way passage The pharmacologist's interest in the problem of intestinal permeation is twofold on the one hand this process determines the bioavailability of drugs and contributes significantly to the pharmacokinetics and toxicokinetics of xenobiotics on the other hand the pharmacodynamic effects of many drugs are manifested in a significant alteration of the physiological process of intestinal permeation **Pharmacology of the Skin II**

,2012-12-06 The recent interest in the pharmacology of the skin and the treatment of its diseases has come about for two reasons The first is a realisation that many aspects of pharmacology can be studied as easily in human skin as in animal models where they may be more relevant to human physiology and disease Examples of this are the action of various vasoactive agents and the isolation of mediators of inflammation after UV irradiation and antigen induced dermatitis The second reason is the fortuitous realisation that a pharmacological approach to the treatment of skin disease need not always await the full elucidation of aetiology and mechanism For example whilst the argument continued unresolved as to whether the pilosebaceous infection which constitutes acne was due to a blocked duct or to a simple increase in sebum production 13 cis retinoic acid was found quite by chance totally to ablate the disease again whilst cyclosporin fresh from its triumphs in organ transplantation has been found able to suppress the rash of psoriasis it has resuscitated the debate on aetiology We are therefore entering a new era in which the pharmacology and clinical pharmacology of skin are being studied as a fascinating new way of exploring questions of human physiology and pharmacology as well as for the development and study of new drugs use of which will improve disease control and at the same time help to define pathological mechanisms

Pharmacology of Intestinal Permeation I ,2012-12-06 The intestine particularly the small bowel represents a large surface in the adult 2 human approximately 200m through which the body is exposed to its environment A vigorous substrate exchange takes place across this large surface nutrients and xenobiotics are absorbed from the lumen into the bloodstream or the lymph and simultaneously the same types of substrate pass back into the lumen The luminal surface of the intestine is lined with a leaky epithelium thus the passage of the substrates in either direction proceeds via both transcellular and

intercellular routes Simple and carrier mediated diffusion active transport pinocytosis phagocytosis and persorption are all involved in this passage across the intestinal wall The term intestinal permeation refers to the process of passage of various substances across the gut wall either from the lumen into the blood or lymph or in the opposite direction Permeability is the condition of the gut which governs the rate of this complex two way passage The pharmacologist s interest in the problem of intestinal permeation is twofold on the one hand this process determines the bioavailability of drugs and contributes significantly to the pharmacokinetics and toxicokinetics of xenobiotics on the other hand the pharmacodynamic effects of many drugs are manifested in a significant alteration of the physiological process of intestinal permeation

Pharmacology of Asthma Clive P. Page, Peter J. Barnes, 2012-12-06 This volume forms part of a prestigious series and covers the latest advances in our understanding of the pathophysiology and treatment of asthma Our understanding of asthma has changed dramatically in recent years and much of this new information is brought together in this volume written by internationally recognised authorities The aim of the book is to review in depth the changing concepts of inflammatory processes in asthma and to discuss the implications for research of this common chronic disease Many of the advances in and future therapy our understanding of asthma have originated from a pharmacological approach and this volume highlights the promising new options for pharmacological intervention It is hoped this book will be invaluable for research scientists and clinicians involved in asthma research and will be a major reference resource for chest physicians and those involved in the development of novel pharmaceutical entities Each chapter is extensively referenced generously illustrated with clear diagrams and photographs and represents a state of the art review of this growing area c P PAGE P J BARNES Contents CHAPTER 1 The Pathology of Asthma An Overview L A LAMNEN and A LAMNEN With 10 Figures 1 A Introduction 1 B Methods to Investigate the Pathology of Human Asthma 1 C Bronchial Epithelium and Inflammatory Cells in Asthmatic Patients Between Attacks 2 I Mast Cells 4 II Eosinophils 7 III Neutrophils 10 D Bronchial Epithelial Inflammation During an Asthma Attack 10 E Epithelial Regeneration 12 Radioimmunoassay in Basic and Clinical Pharmacology Carlo

Patrono, Bernhard A. Peskar, 2012-12-06 Thirty years have elapsed since the first description by S A BERNSON and R S YALOW of the basic principles of radioimmunoassay RIA During this period of time RIA methodology has been instrumental to the growth of many areas of biomedical research including endocrinology oncology hematology and pharmacology It has done so by providing a relatively simple universal tool allowing for the first time the detection of endogenous mediators that are present in body fluids at concentrations as low as 10^{-10} M The fundamental nature of this discovery and the wide ranging fall out of basic and clinical knowledge derived from its application have been acknowledged by the many honors tributed to its pioneers including the Nobel Prize awarded to Dr YALOW 10 years ago Although several excellent books have been published during the past decades covering various aspects of RIA methodology we felt the need as pharmacologists for a comprehensive discussion of the methodological and conceptual issues related to the main classes of mediators of drug

action and to drugs themselves Thus we gladly accepted the challenge provided by the invitation to edit a volume of the Handbook of Experimental Pharmacology on Radioimmunoassay in Basic and Clinical Pharmacology We tried to balance the emphasis placed on more general aspects of the RIA methodology and that on specific mediators Local Anesthetics Gary R. Strichartz, 2012-12-06 Local anesthetics are among the most widely used drugs Their development over the past century ranges from a documented influence on Freud's Interpretation of Dreams 1 to the synthesis of the ubiquitously popular lidocaine as described in Chapter 1 For surgical procedures the use of regional epidural and intrathecal local anesthesia has increased continuously during the past decade Local anesthetics are also applied by physicians to ameliorate unpleasant sensations and reactions to other procedures such as tracheal intubation The presence or the threat of cardiac arrhythmias is often countered by chronic administration of local anesthetic like agents such as lidocaine or procainamide Relief of acute pain accompanying dental manipulations for example and of chronic pain are also accomplished with traditional local anesthetics And over the counter formulations of topical local anesthetics provide practitioners of solar indiscretion welcome relief from their otherwise unaccommodating sunburn In all these applications the final effect of the local anesthetic is an inhibition of electrical activity accomplished as a reduction or total blockade of action potentials The primary site of action is the sodium channel a transmembrane protein which is essential for the influx of sodium ions that subserves impulse generation and propagation in nerves skeletal muscle and heart The detailed mechanisms of local anesthetic action are still being investigated and Chapter 2 of this volume provides a current overview of that subject **Histamine and Histamine Antagonists** Börje Uvnäs, 2012-12-06 Together with the two previous volumes of the Handbook of Experimental Pharmacology on histamine and antihistamines the present publication yields a picture of a still rapidly developing field of research New techniques and new experimental approaches have brought us new knowledge and deeper insight into the biomedical significance of histamine even if many questions remain to be answered about the functional and medical implications of this old biogenic amine The present volume covers the progress in histamine research during the past two decades A significant chapter concerns techniques for histamine determination As the result of a consensus meeting in Munich in December 1988 a panel of eminent specialists arrived at common recommendations as to the usefulness of the available histamine assays for the most common experimental biomedical conditions The heterogeneity of mast cells with great differences in their reactivity to various stimuli has become apparent not only among species but also among the tissues of a species New information is presented about the mechanism of exocytosis The old questions about the role of histamine in the mechanism of gastric secretion and in cardiovascular and respiratory functions have been studied with new techniques and the role of H₁ and H₂ receptors discussed New observations have been made on the occurrence and possible functions of histaminergic neurons and histamine receptors in CNS where a new type of receptor the H₃ seems to be widely represented Glucagon II , 2012-12-06 The Pharmacology of Lymphocytes Michael A. Bray, John Morley, 2012-12-06

Immunopharmacology why not pharmacimmunology Professor H O Schild University College London 1962 An intact immune response is essential for survival as is evidenced by the various innate immune deficiency syndromes and by the emergence of the acquired immune deficiency syndrome AIDS as a pandemic during the last decade Substances which stimulate the immune response might contribute to the therapy of AIDS and its precursor AIDS related syndrome as well as of other clinical conditions in which immune responses can be diminished such as carcinoma and infections In other circumstances an intact or heightened immune response may pose clinical problems hence there is need to suppress or diminish components of the immune response For instance it is necessary to impair cellular immunity in order to ensure lasting acceptance of heterografts and it is already established that agents effective in transplantation are therapeutically effective in an range of autoimmune diseases More recently experimental studies have indicated that aberrant manifestations of humoral immunity as in allergies may also be amenable to pharmacological intervention

The Cholinergic Synapse
Victor P. Whittaker, 2012-12-06 One of the most impressive works of scholarship in the field of experimental pharmacology has been the Heffter Heubner Handbuch der experimentellen Pharmakologie internationalized some years ago under the title Handbook of Experimental Pharmacology and kept up to date by a series of numbered Ergänzungswerke or supplementary volumes which have now replaced in importance the original Handbuch These volumes constitute a valuable and continuously up dated multi author review series of topics important in modern pharmacology and allied sciences The Editorial Board of the Handbook invited me 2 years ago to undertake as subeditor the preparation of a new volume entitled The Cholinergic Synapse A previous volume in this series vol 15 Cholinesterases and Anticholinesterase Agents edited by GEORGE KOELLE was published in 1963 and was far wider in scope than its title suggested it was in fact an authoritative summing up of the whole subject of cholinergic function and still has some value today as an account of the state of the art as it was at that time Since then another excellent review of a specific cholinergic synapse has appeared in this series this was vol 42 Neuromuscular Junction edited by ELEANOR ZAIMIS and published in 1976 A third volume vol 53 Pharmacology of Ganglionic Transmission which appeared in 1980 and was edited by D A KHARKEVICH includes important aspects of autonomic cholinergic function

Mediators and Drugs in Gastrointestinal Motility II, 2012-12-06 This volume places more emphasis on endogenous mediators of gut motility than on drugs used to treat patients with deranged motility In this respect it resembles most other books on gastroenterology for while only a relatively small number of drugs are really useful for a rational therapy a tremendous amount of data is available on neural and hormonal factors regulating the motility of the alimentary canal Moreover it must be considered that some of the drugs which can routinely be employed to modify deranged motility of the digestive system are represented by pure or slightly modified endogenous compounds e g cholecystokinin its C terminal octapeptide and caerulein and it is easy to foresee that their number is destined to increase in the near future Other drugs are simply antagonists of physiological substances acting on specific receptors e g histamine H

blockers 2 and opioid compounds The real explosion of research in this field and the extreme specialization often connected with the use of very sophisticated techniques and methodologies would probably have required a larger number of experts to cover some very specific fields from both an anatomical lower esophageal sphincter stomach pylorus small and large intestine and a biochemical hormones candidate hormones locally active substances neurotransmitters etc point of view

Antimalarial Drug II ,2012-12-06 The construction of this volume has been guided by two personal convictions Experience in the field of experimental chemotherapy both in the pharmaceutical industry and academia has convinced us that recent quantum technological advances in biochemistry molecular biology and immunology will permit and indeed necessitate an increasingly greater use of rational drug development in the future than has been the custom up to now In Part I therefore we asked our contributors to provide detailed reviews covering the biology of the malaria parasites and their relation with their hosts the experimental procedures including culture techniques that are necessary to take a drug from primary screening to clinical trial and an account of antimalarial drug resistance Our second conviction is that many research workers are all too loath to learn from the lessons of the past For this reason we asked the contributors to Part 2 of this volume to review very thoroughly the widely scattered but voluminous literature on those few chemical groups that have provided the antimalarial drugs in clinical use at the present time Much can be learned from the history of their development and the problems that have arisen with them in man Some indeed may still have much to offer if they can be deployed in better ways than they are at present This question has been taken up by several authors **Mediators and Drugs in**

Gastrointestinal Motility I ,2012-12-06 Since the exhaustive Handbook of Physiology Alimentary Canal Section 6 Motility edited by CHARLES F CODE in 1968 no complete survey of the morphological basis and the physiological control of intestinal motility has been published in spite of the enormous amount of new data in the literature on this topic The new techniques and methodologies the use of electron microscopy radioimmunoassay and binding techniques as well as ever more sophisticated electrophysiological procedures have made possible areal flood of discoveries in this field Moreover the possibility of new studies of the endocrine cells in biopsies of human intestinal mucosa even during routine endoscopies has opened new horizons for gastroenterologists and generated a number of important contributions to our knowledge of the morphology and physiopathology of the gut As usual new discoveries have also revealed both ignorance and many new problems For this reason although many of the data reported in this volume can be considered as firmly established others still require confirmation and the results of new research in this field are awaited with extreme interest Since advances are occurring so rapidly even experts in the specific topics need frequent comprehensive reviews To avoid an excessively large volume considerations of the pancreas liver and biliary system were not included in this Handbook which nevertheless has attempted to offer the reader the essence of more than 1 500 papers **Polish Journal of Pharmacology and Pharmacy**

,1983 **Antibiotics** ,2012-12-06 Teratogenesis and Reproductive Toxicology E.M. Johnson,D.M. Kochhar,2012-12-06

The resolution of links between exposure to components of our complex environmental and causation of reproductive effects in the population constitutes an important problem in the field of toxicology. The focus of this volume is developmental toxicology which represents one aspect of reproductive toxicology dealing with the study of adverse effects on the developing conceptus. Developmental toxicology which includes teratogenesis as one of its manifestations provides a fertile field for research in several basic and clinical disciplines. This field also receives input from several disciplines such as developmental and molecular biology, pathology, pharmacology and toxicology, pediatrics and neonatology and epidemiology. More recently we have seen an emergence of interest in other fields such as perinatal physiology and postnatal behavior which have now become incorporated into the mainstream of research in this discipline. The present volume is an effort to provide a sampling of concepts currently under active investigation in several of the above fields. The authors have endeavored to provide up to date information on the following topics: detection and analysis of potential hazards to the conceptus in the workplace; pharmacokinetic aspects of the maternal-placental-fetal complex and its relationship to human birth defects and probable mechanisms of teratogenesis as uncovered in certain well defined situations. Also included are summaries of newer investigations on the emerging field of postnatal functional evaluations i.e. adverse effects on adult activities resultant from in utero exposure to toxic substances.

Toxicology of Inhaled Materials H.P. Witschi, J.D. Brain, 2012-12-06 This book deals with the methods and scientific basis of inhalation toxicology. It describes devices and facilities needed to expose animals to inhaled particles and gases as well as approaches to estimating or measuring the fraction of the inhaled material that is retained in the respiratory tract. The book then reviews the evergrowing repertoire of techniques that can be used to measure the responses elicited by the exposure. Quantitative and qualitative anatomical, physiological and biochemical strategies are discussed in detail. We believe that the toxicology of inhaled materials is an important and timely topic for several reasons. During the past decade morbidity and mortality attributable to cardiovascular disease have significantly decreased. Progress in combatting cancer, the second most important cause of death, has been slower and lung cancer actually became the leading cause of death in men and the second leading cause of cancer death in women. In addition, the incidence of non-neoplastic respiratory diseases such as emphysema, fibrosis and chronic bronchitis has increased the past decade. In the United States the National Institutes of Health (NIH) has recently reported that chronic obstructive pulmonary disease affects nearly 10 million persons and accounts for 59,000 deaths yearly; indeed it ranks as the fifth leading cause of death. Because the incidence is increasing, the NIH estimates that it may become the nation's fourth or even third leading cause of death by the year 2000.

Glucagon I, 2012-12-06 The Editorial Board of the Handbook of Experimental Pharmacology apparently did not hurry in suggesting production of a volume on glucagon since the present opus is number sixty-six in the series. This fact is even more striking if we consider that 34 volumes published over about eight years will separate the books on glucagon from those on insulin on library shelves whereas only a few microns separate the cells manufacturing these two polypeptides.

within the islets of Langerhans in the pancreas Numerous factors have probably caused this discrimination four of them are First insulin deficiency or resistance is the cause of one of the most serious and distressing diseases diabetes mellitus which affects millions of people whereas glucagon deficiency is apparently an extremely rare disorder for which detailed reports are published of individual cases whenever they occur Second since its discovery in 1921 by BANTING and BEST insulin has been irreplaceable for the treatment of the most severe forms of diabetes whereas in contrast glucagon was until recently considered a relatively minor therapeutic agent Third whereas insulin is a compound which has been well characterized since the pioneering work of SANGER and its biosynthesis clearly identified by STEINER and his co workers glucagon also well characterized chemically has suffered from its parenthood with the so called glucagon like immunoreactive substances an incompletely defined series of immunologically related polypeptides present in the gut the pancreas and some other parts of the body

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Introduction

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