NEW ANTIHYPERTENSIVE DRUGS

Edited by ALEXANDER SCRIABINE and CHARLES S. SWEET

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Alexander Scriabine, M.D.

and

Charles S. Sweet, Ph.D.

Merck Institute for Therapeutic Research
West Point, Pennsylvania

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Contributors

WILLIAM B. ABRAMS, M.D.[1]
Clinical Research
Ayerst Laboratories
685 Third Avenue
New York, New York

MICHAEL J. ANTONACCIO, Ph.D.
Pharmaceuticals Division
Ciba-Geigy Corporation
Summit, New Jersey

DOMINGO M. AVIADO, M.D.
Department of Pharmacology
University of Pennsylvania
Medical School
Philadelphia, Pennsylvania

TIBOR BALAZS, D.V.M.
Pharmaceutical Research and Testing
Bureau of Drugs
Food and Drug Administration
Washington, D.C.

THOMAS BAUM, Ph. D.
Department of Pharmacology
Wyeth Laboratories, Inc.
Philadelphia, Pennsylvania

BARRY A. BERKOWTIZ, Ph.D.
Department of Physiological Chemistry
Roche Institute of Molecular Biology
Nutley, New Jersey

ROGER BOUCHER, Ph.D.
Clinical Research Institute of Montreal
Montreal, Canada

MICHAEL J. BRODY, Ph.D.
Department of Pharmacology
University of Iowa
College of Medicine
Iowa City, Iowa

[1]Present Address: Merck Sharp & Dohme Research Laboratories, West Point, Pennsylvania 19486.

CONTRIBUTORS

WILLIAM B. CAMPBELL, Ph.D.[2]
Department of Internal Medicine
University of Texas
Health Science Center
Dallas, Texas

MARLENE H. COHEN, Ph.D.[3]
Roche Institute of Molecular Biology
Nutley, New Jersey

DAVID DEITCHMAN, Ph.D.
Department of Biological Research
Mead Johnson Research Center
Evansville, Indiana

A. DORNIER, M.D.
Clinical Research Institute of Montreal
Montreal, Canada

KENNETH L. DUCHIN
Department of Pharmacology
College of Medicine and Dentistry of
New Jersey
New Jersey Medical School
Newark, New Jersey

F. L. EARL, D.V.M.
Department of Health, Education and
Welfare
Food and Drug Administration
Washington, D.C.

STEWART J. EHRREICH, Ph.D.
Department of Pharmacology
Schering Corporation
Bloomfield, New Jersey

GEORGE M. FANELLI, Ph.D.
Department of Pharmacology
Merck Institute for Therapeutic Research
West Point, Pennsylvania

MICHAEL FERNANDES, M.D.
Department of Medicine
Hahnemann Medical College
Philadelphia, Pennsylvania

WALTER A. FREYBURGER, Ph.D.
Cardiovascular Diseases Research
The Upjohn Company
Kalamazoo, Michigan

EDWARD D. FROHLICH, M.D.
Department of Medicine
University of Oklahoma
Health Sciences Center
Oklahoma, City, Oklahoma

JACQUES GENEST, M.D.
Clinical Research Institute of Montreal
Montreal, Canada

THEODORE L. GOODFRIEND, M.D.
Departments of Medicine and
Pharmacology
University of Wisconsin
Center for Health Sciences
Madison, Wisconsin

JEANNE HALLEY
Pharmacueitcals Division
Ciba-Geigy Corporation
Summit, New Jersey

A. HEISE, M.D.
Institute of Pharmacology
Bayer AG
West Germany

E. HERMAN, Ph.D.
Department of Health, Education and
Welfare
Food and Drug Administration
Washington, D.C.

WOLFGANG HOEFKE, M.D.
Department of Pharmacology
C. H. Boehringer Sohn
Ingelheim, West Germany

[2]Present Address: Medical College of Wisconsin, Milwaukee County Medical Complex, Milwaukee, Wisconsin 53226.
[3]Present Address: The Lilly Research Laboratories, Eli Lilly & Co., Indianapolis, Indiana 46206.

LORENZ M. HOFMANN, Ph.D.
Department of Biological Research
Searle Laboratories
Chicago, Illinois

DUNCAN E. HUTCHEON, M.D., D. Phil.
Department of Pharmacology
College of Medicine and Dentistry of New Jersey
New Jersey Medical School
Newark, New Jersey

HAROLD D. ITSKOVITZ, M.D.
Medical College of Wisconsin
Milwaukee County Medical Complex
Milwaukee, Wisconsin

P. JERIE
Biological and Medical Research
Sandoz Ltd.
Basle, Switzerland

EUGENE M. JOHNSON, JR., Ph.D.
Department of Pharmacology
Medical College of Pennsylvania

GERALD J. KELLIHER, Ph.D.
Department of Pharmacology
Medical College of Pennsylvania
Philadelphia, Pennsylvania

CHRYZANTA A. KORDUBA
Department of Biochemistry
Schering Corporation
Bloomfield, New Jersey

O. KUCHEL, M.D., D.Sc.
Clinical Research Institute of Montreal
Montreal H2W 1R7
Canada

L. T. LAIS, Ph.D.
Department of Pharmacology
University of Iowa
College of Medicine
Iowa City, Iowa

JOHN H. LARAGH, M.D.
Cardiovascular Center and Hypertension Center
The New York Hospital
Cornell Medical Center
New York, New York

CARL T. LUDDEN
Department of Pharmacology
Merck Institute for Therapeutic Research
West Point, Pennsylvania

WILLIAM B. MARTIN, M.D.
Research Laboratories
The Upjohn Company
Kalamazoo, Michigan

GORDON R. MCKINNEY, Ph.D.
Department of Biologic Research
Mead Johnson Research Center
Evansville, Indiana

W. NOWACZYNSKI, D.Sc.
Clinical Research Institute of Montreal
Montreal, Canada

GADDO ONESTI, M.D.
Division of Nephrology and Hypertension
Hahnemann Medical College
Philadelphia, Pennsylvania

MELVILLE, W. OSBORNE, Ph.D.
Department of Pharmacology
Hoffmann-La Roche, Inc.
Nutley, New Jersey

IRVINE H. PAGE, M.D.
Research Division
The Cleveland Clinic Foundation
Cleveland, Ohio

JAMES L. PERHACH, JR., Ph.D.
Department of Biologic Research
Mead Johnson Research Center
Evansville, Indiana

CONTRIBUTORS

WILLIAM A. PETTINGER, M.D.
Department of Pharmacology
University of Texas
Health Science Center
Dallas, Texas

MARC A. PFEFFER, Ph.D.
Division of Hypertension
Department of Medicine
The University of Oklahoma
Health Sciences Center
Oklahoma City, Oklahoma

ROBERT POCELINKO, M.D.
Department of Pharmacology
College of Medicine and Dentistry of
New Jersey
New Jersey Medical School
Newark, New Jersey

T. P PRUSS, Ph.D.
Department of Pharmacology
McNeil Laboratories, Inc.
Fort Washington, Pennsylvania

OWEN G. REESE, JR., M.D.
Department of Medicine
University of Wisconsin
Center for Health Sciences
Madison, Wisconsin

RONALD D. ROBSON, Ph.D.
Pharmaceuticals Division
Ciba-Geigy Corporation
Summit, New Jersey

J. M. ROJO-ORTEGA, M.D., Ph.D.
Clinical Research Institute of Montreal
Montreal, Canada

HORACE F. RUSSO
Department of Pharmacology
Merck Institute for Therapeutic Research
West Point, Pennsylvania

HARRY SALEM, Ph.D.
Department of Pharmacology
University of Pennsylvania
Medical School
Philadelphia, Pennsylvania

G. SCHOLTYSIK, M.D.
Biological and Medical Research
Sandoz Ltd.
Basle, Switzerland

ALEXANDER SCRIABINE, M.D.
Department of Pharmacology
Merck Institute for Therapeutic Research
West Point, Pennsylvania

ALLEN T. SHROPSHIRE
Department of Pharmacology
Wyeth Laboratories, Inc.
Philadelphia, Pennsylvania

THOMAS H. STEELE, M.D.
Department of Medicine
University of Wisconsin
Center for Health Sciences
Madison, Wisconsin

CHARLES S. SWEET, Ph.D.
Department of Pharmacology
Merck Institute for Therapeutic Research
West Point, Pennsylvania

ALFONSO J. TOBIA, Ph.D.
Department of Pharmacology
Smith Kline and French Laboratories
Philadelphia, Pennsylvania

GERALD M. WALSH, Ph.D.
Department of Medicine
University of Oklahoma
Health Sciences Center
Oklahoma City, Oklahoma

L. SHERMAN WATSON, Ph.D.
Department of Pharmacology
Merck Institute for Therapeutic Research
West Point, Pennsylvania

HERBERT C. WENGER
Department of Pharmacology
Merck Institute for Therapeutic Research
West Point, Pennsylvania

GERALD R. ZINS, Ph.D.
Research Laboratories
The Upjohn Company
Kalamazoo, Michigan

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NEW ANTIHYPERTENSIVE DRUGS

Introduction

This volume represents the edited version of the seventeenth Alfred Newton Richards Symposium sponsored by The Physiological Society of Philadelphia and held on May 19-20, in King of Prussia, Pennsylvania. This volume is dedicated to Dr. A. N. Richards whose research greatly contributed to our present understanding of renal function.

The symposium reflected the significant progress made during the last few years in the basic knowledge of the pathogenesis of hypertension as well as in the development of new antihypertensive drugs. The recognition of the necessity to treat moderate or even mild hypertension has created an increased demand for antihypertensive drugs. The long-term therapy of hypertension has led to a greater awareness of the side effects of presently available antihypertensive drugs and to the recognition that safer drugs are needed.

To develop novel therapeutic approaches to hypertension, the greatest possible interaction is needed between our leaders in academic hypertension research and pharmacologists able to apply ideas to new drug developments. This symposium represented a forum for such

interaction. In the past, pharmacologists have made significant contributions to the therapy of hypertension which drastically decreased the morbidity and mortality of hypertensive patients. It is remarkable that diuretics were developed and used in the treatment of hypertension before "volume" hypertension became a popular term and that inhibitors of the sympathetic nervous system were used long before the term "vasoconstrictor" hypertension was proposed. Pharmacologists have also provided substances which were useful in the elucidation of the pathogenesis of hypertension. This included peripheral and central inhibitors of the sympathetic nervous system and inhibitors of the renin-angiotensin system.

Future progress in the development of new drugs will not be achieved by one single scientist or one laboratory. Collaborative efforts between academic research, industrial pharmacology and government agencies will be required. The importance of the efforts of scientists from government agencies should not be underestimated; they are in an excellent position to contribute constructively to the development and availability of new antihypertensive drugs in this country.

The new concepts in hypertension research, discussed in this volume, are:

1. "Volume" hypertension and diuretics.
2. "Vasoconstrictor" hypertension and the renin-angiotensin system.
3. Cyclic nucleotides and hypertension.
4. Control of arterial pressure by central α-adrenergic, β-adrenergic and dopaminergic receptors.
5. Peripheral vasodilators as an integral part of logical combination therapy.

Numerous new drugs and even new classes of drugs were introduced or evaluated in the therapy of hypertension. This includes:

1. Diuretics — indanones, bumetanide, new aldosterone antagonists, tienilic acid, metolazone, indapamide.
2. Stimulants of central α-adrenergic receptors — clonidine, xylazine, guanabenz, BS 100/141, tiamenidine.
3. α-Adrenergic blocking drugs—indoramin, prazosin.
4. β-Adrenergic blocking drugs — propranolol, alprenolol, oxprenolol, sotalol, practolol, timolol, tolamolol, acebutolol, pindolol, and many others.
5. Dopamine-β-hydroxylase inhibitors — fusaric acid, bupicomide.
6. Norepinephrine-depleting drugs — MJ 10459-2.
7. Inhibitors of the renin-angiotensin system — SQ 20881, saralasin.

8. Peripheral vasodilators — minoxidil, nifedipine, SKF-24260, ISF 2123, L 6150.

Of considerable importance for the research in hypertension was the introduction of the Okamoto-Aoki strain of spontaneously hypertensive rats as a model of essential hypertension. During the last decade, these animals have become a highly useful tool in hypertension research. Their responsiveness to currently used antihypertensive drugs was found to be very similar to that of essentially hypertensive man. New methods of continuous direct recording of arterial pressure in these animals permitted studies of chronic effects of potential antihypertensive drugs. Attempts were also made to evaluate the possible effectiveness of drugs on the development of hypertension in younger animals.

The search for new centrally acting antihypertensive drugs led to the development of methodology of drug administration to various areas of the central nervous system. These methods are discussed in the contributions of Antonaccio and Halley; Heise; Scholtysik and Jerie; and Sweet, et al.

Future trends in hypertension research can now be identified as follows:

1. Search for further factors responsible for the development of hypertension.
2. Further elucidation of biochemical abnormalities in hypertension and attempts at their prevention.
3. Search for novel centrally acting antihypertensive drugs with minimal side effects.
4. Elucidation of the role of prostaglandins in the pathogenesis and treatment of hypertension.
5. Evaluation of the effects of drugs on the morbidity and mortality of hypertensive animals.

These trends are suggested by various contributors to this volume.

A. Scriabine
C. S. Sweet

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