Prostaglandins in Clinical Medicine

Cardiovascular and Thrombotic Disorders

KENNETH K. WU
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PROSTAGLANDINS IN CLINICAL MEDICINE

CARDIOVASCULAR AND THROMBOTIC DISORDERS

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Proceedings of an International Symposium
"Prostaglandins in Cardiovascular and Thrombotic Disorders"
Chicago, Illinois, May 7–9, 1981

YEAR BOOK MEDICAL PUBLISHERS, INC.
Chicago • London

Library of Congress Cataloging in Publication Data
Main entry under title:

Prostaglandins in clinical medicine.

Includes index.
1. Cardiovascular system—Diseases—Chemotherapy—Congresses. 2. Prostaglandins—Therapeutic use—Congresses. 3. Thrombosis—Chemotherapy—Congresses. I. Wu, Kenneth K. II. Rossi, Ennio C.
[DNLM: 1. Prostaglandins—Therapeutic use—Congresses. 2. Prostaglandins—Pharmacodynamics—Congresses. 3. Cardiovascular diseases—Drug therapy—Congresses. 4. Thrombosis—Drug therapy—Congresses. 5. Lung diseases—Drug therapy—Congresses. QU 90 P969 1981]
RC684.P76P76 616.1'061 81-23995
ISBN 0-8151-9609-1 AACR2

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Preface

Fifty-one years ago, human seminal fluid was shown to produce contraction of smooth muscle. Von Euler found this activity in extracts of the prostate gland and named the active principle "prostaglandin." These early observations, which introduced a new era, did not receive much attention for two decades. Subsequently, however, prostaglandins have been characterized, and their biological actions have been well described. They appear to play an important role in the regulation of many physiologic systems, and the steady flow of new information continually broadens the arena in which prostaglandins appear to act. Important clinical applications seem inevitable.

On the 7th, 8th, and 9th of May, 1981, an international symposium sponsored by Rush Medical College and the Northwestern University School of Medicine, was held in Chicago to explore the clinical applications of prostaglandins in cardiovascular and thrombotic disorders. This volume contains the proceedings of that symposium. The first two sections deal with the basic principles and physiologic effects of prostaglandins. They are followed by sections that describe clinical trials of prostaglandins in peripheral vascular and coronary artery disease; their potential role in asthma, persistent fetal pulmonary circulation, and thrombotic disorders; and the use of prostacyclin in cardiopulmonary bypass surgery.

Frequently, the goal of symposia proceedings is limited to the gathering and organization of previously published information. We believe these proceedings may exceed this limitation. Because of the rapid progress in prostaglandin research, a significant amount of the information presented—especially on clinical trials—is new. We hope the reader will share our view that the clinical data obtained to date confirm the promise of prostaglandin research and foreshadow clinical applications yet to come.

ACKNOWLEDGMENTS

We wish to thank Drs. Udo Axen, Edmond Cole, Francesco del Greco, John Phair, and Max Rafelson for their assistance in organizing the symposium that led to these proceedings. We also express our gratitude to the Upjohn Company, Kalamazoo, Michigan and to the Division of Blood Diseases and Resources of the National Heart, Lung, and Blood Institute for financial support; and to Dr. Harold Paul, Dr. Joseph Vaal, and the staff of Rush-Presbyterian-St. Luke's Medical Center Office of Continuing Education for logistic support. Finally, we wish to express our special appreciation to the investigators who participated in the symposium and provided manuscripts for these proceedings.

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PART I

BASIC PRINCIPLES OF PROSTAGLANDINS

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Lipids, Membranes, and Essential Fatty Acids

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Introduction

Lipids can be broadly defined as a chemically heterogeneous group of biomolecules with the common property of insolubility in water but solubility in nonpolar solvents.[1] In this chapter, we will mainly confine our discussion to lipids that are esters of long-chain fatty acids. Three major classes of lipids contain esterified fatty acids: phospholipids, glycolipids, and neutral lipids.[1]

Phospholipids serve as structural components in mammalian cells and tissues. In addition, phospholipids can be conceived as metabolic storage depots for essential fatty acids (EFA). Some phosphoglycerides, such as phosphatidyl-inositol (PI) and phosphatidic acid (PA), turn over rapidly when the cell is stimulated.[2] Tissue fractionation studies have indicated that phospholipids in subcellular compartments usually have similar fatty acid compositions.[3] These similarities may relate to a requirement of phospholipids for normal cell structure and function. Turnover of intact phosphoglyceride molecules is slow. Only the fatty acid moiety is renewed rapidly by intracellular fatty acid transfer. Although arachidonate is the precursor of prostaglandins and hydroxy acids, it may also lend a certain degree of stability to phospholipid components in cell membranes.

Glycolipids contain one or more sugar molecules, and some also have a sialic acid moiety (gangliosides). In human platelets the major