

The Artery and the Process of Arteriosclerosis

Measurement and Modification

ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY

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The Artery and the Process of Arteriosclerosis Measurement and Modification

The second half of the Proceedings of an Interdisciplinary Conference on Fundamental Data on Reactions of Vascular Tissue in Man, April 19-25, 1970, Lindau, West Germany

Edited by

Stewart Wolf

*University of Texas System Professor of Medicine
Professor of Medicine and of Physiology
The University of Texas Medical Branch and
Director, The Marine Biomedical Institute
Galveston, Texas*

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The first half of the proceedings was published as
The Artery and the Process of Arteriosclerosis: Pathogenesis
(Volume 16A of this series).

Library of Congress Catalog Card Number 70-163284

ISBN-13: 978-1-4615-8227-4

e-ISBN-13: 978-1-4615-8225-0

DOI: 10.1007/978-1-4615-8225-0

© 1972 *Plenum Press, New York*

Softcover reprint of the hardcover 1st edition 1972

A Division of Plenum Publishing Corporation

227 West 17th Street, New York, N.Y. 10011

United Kingdom edition published by Plenum Press, London

A Division of Plenum Publishing Company, Ltd.

Davis House (4th Floor), 8 Scrubs Lane, Harlesden, London, NW 10 6SE, England

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DEDICATION

This volume is dedicated to the memory of Dr. Theodore Gillman who died July 12, 1971, before he had a chance to edit his remarks that are a part of the record of proceedings published herein. Dr. Gillman worked very hard over his material and contributed mightily to the Conference. His fresh, energetic and imaginative approach to the unravelling of the mysteries of arteriosclerosis will be greatly missed.

PREFACE

Substantial progress toward reconciling disparate theories of the pathogenesis of arteriosclerosis was recorded in Volume I of this book, the proceedings of an interdisciplinary workshop conference held at Lindau, Germany, April 19-25, 1970. Strong evidence was adduced that the early stages of arteriosclerosis consist of intimal proliferation similar to that associated with the increase in arterial size and caliber that characterizes normal growth. The findings described recall a theory proposed by Richard Thoma (Thoma and Kaefer, 1889) of Heidelberg toward the end of the nineteenth century. He suggested that the pathogenesis of arteriosclerosis began with intimal thickening that was initially adaptive. Past a certain point, however, the thickening compromised the nutrition of the artery wall, leading inevitably to degenerative changes.

In 1944 Hueper (Hueper, 1944), reemphasized the threat to the nutritional support of the artery and proposed that the many etiologic factors capable of inducing arterial atheroma did so through the final common pathway of interfering with oxidative mechanisms in the vessel wall. Thus, it is proposed that arteriosclerosis is basically an aspect of the "behavior" of the artery. The nature of the lesion, therefore, depends more on the biochemical and structural response capabilities of the tissue itself than on the characteristics of the various etiologic agents. The idea that arteriosclerosis begins as uncontrolled or disturbed adaptive behavior was shared by Duff and also by Winternitz (Duff, 1954; Winternitz, 1954). Henry Moon (Moon, 1967) sums up this point of view in his chapter in Cowdry's Arteriosclerosis: "the frequency with which sclerotic alterations are seen in arteries from individuals of all ages suggests that early changes result from essentially normal adaptive reactions and that far advanced lesions represent a distortion of this adaptive mechanism."

Although the concept of arteriosclerosis as consisting basically of an adaptive proliferative process in the wall of the artery can explain observed effects of a good many diverse forces that have been reliably incriminated, such as elevated intravascular pressure, hypoxia, immunologic insult and cholesterol feeding, it fails to take into account the possible role of intraluminal structures, especially the platelets. This apparent hiatus in the theory was pointed out in the preceding volume. Evidence was brought forward that platelets may adhere to the endothelial lining after certain chemical "insults" or other subtle injuries. Whether or not they may adhere to perfectly normal healthy endothelium has not been established, although Wojcik, et al., have shown that platelets actually enter the endothelial cells of capillaries and provide support against capillary "fragility" (Wojcik and VanHorn et al., 1969). The conferees offered evidence that, when adherent, the platelet may induce chemical changes in the intima, possibly even increased lipid absorption to support enhanced metabolic demands.

The format of the proceedings does not follow precisely that of the Conference itself. The formal papers are included, somewhat abbreviated, and excerpts of the discussion have been gathered under a series of topics arranged in logical sequence. Therefore, the quoted statements do not necessarily appear in order or in the place in the program where they were made. Principal issues, syntheses and unanswered questions are interspersed among the topics as editorial comments.

The Lindau Conference took place less than six months after the Second International Symposium on Atherosclerosis in Chicago (Atherosclerosis, Proceedings of the Second International Symposium, Edited by Richard J. Jones, Springer-Verlag, New York, Heidelberg, Berlin 1970). Despite the proximity in time and the substantial overlap in participants, the Lindau meeting reflected a further step in understanding the pathogenesis of arteriosclerosis. Each presentation of data was exposed to a more or less leisurely examination and critical comment by interested participants of varying background and experience. Unfortunately, the remarks of some of the participants did not come through clearly enough in the tape recording of the Conference to enable them to be transcribed and included in the Proceedings. Apologies are therefore offered to these contributors. The full list of participants follows:

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The expenses of the Conference and of the preparation of the Proceedings were covered by generous contributions from the following organizations and firms:

Alabama Heart Association
American Heart Association
British Heart Fund
Fannie E. Rippel Foundation
Federal Republic of Germany
City of Lindau
Office of Naval Research
Oklahoma Medical Research Foundation
University of Heidelberg
University of Texas Medical Branch at Galveston
Ayerst Laboratories
Bayer A.G.
Boehringer Mannheim GmbH
CIBA A.G.
CIBA Pharmaceutical Company
Deutsche Maizena Werke GmbH
Farbwerke Hoechst A.G.
Hoffman-LaRoche A.G.
Imperial Chemical Industries
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Merck, Sharp and Dohme Research Laboratories
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Sandoz A.G.
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G.D. Searle and Co.
Smith, Kline and French Foundation
Squibb and Sons Pharmaceutical
Unilever Research Laboratories
Upjohn Company
Warner-Lambert Foundation

In the present volume, which concludes the report of the Lindau Conference, the disparate factors capable of aggravating or complicating the process of arteriosclerosis are brought into focus by way of the same sort of free interchange among disciplines that characterized the earlier discussion at the Conference. The potential therapeutic value of exploring arterial regulatory mechanisms as they relate to intimal proliferative changes and to tissue repair is emphasized and there is considerable speculation concerning the remarkable inter- and intra-species variability in susceptibility to naturally occurring and to experimental arteriosclerosis. In its concluding session, the Conference covered in detail the effects of drugs and other therapeutic maneuvers designed to prevent arteriosclerosis and sudden death. As in the first volume, the final chapter attempts to synthesize the highlights of what has gone before.

The two volumes of these proceedings owe much to Miss Jane Henson who played a major role in planning, in the success of the Conference itself and in the preparation of the material for publication.

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