Contents

List of Contributing Authors ................................................... VII
Homburger, F. (Cambridge, Mass.): Introductory Remarks................... X

I. Introduction
Reiser, S. J. (Boston, Mass.): The Patient’s Insight: Its Role in the Evolution of Cardiology................................................................. 2
Wissler, Robert W. (Chicago, 111.): Atherosclerosis - Its Pathogenesis in Perspective 10
Abelmann, W. H. (Boston, Mass.): Cardiovascular Dynamics: A Broad View .... 32

II. Spontaneous Cardiomyopathies

A. Human

Harris, L. C. (Galveston, Tex.): Newer Aspects of Cardiomyopathies.......... 44
Herman, M. V.; Gorlin, R., and Kreulen, T. H. (Boston, Mass.): Ventriculographic Classification of Primary Myocardial Disease............... 53

B. Animals

Hadlow, W. J. (Hamilton, Mont.): Myopathies of Animals - A Brief View........... 68
Owens, K.; Weglicki, W. B. ; Ruth, R. C., and Sonnenblick, E. H. (Boston, Mass.): Abnormalities of Myopathic Subcellular Fractions: Composition and Function.............................................................. 81
Gainer, J. H. (Rockville, Md.): Viral Myocarditis in Animals............... 94

Contents VI

III. Atheromatosis

Luginbühl, H. and Pauli, B. (Bern); Ratcliffe, H. L. (Philadelphia, Pa.): Atherosclerosis
in Swine and Swine as a Model for the Study of Atherosclerosis_ 119
Morrison, E. S. and Scott, R. F. (Albany, N.Y.) : Arterial Wall Metabolism in
Experimental Atherosclerosis .................................................. 127
Bullock, B.C. (Winston-Salem, N.C.): Atherosclerosis in Pigeons and Squirrel
Monkeys ............................................................................. 134
Ratcliffe, H. L. (Philadelphia, Pa.): Social Factors and Atherosclerosis ........ 141
Zook, B. C. (Washington, D.C.): Some Spontaneous Cardiovascular Lesions in
Dogs and Cats .................................................................. 148
Renaud, S. (Lyon-Bron): Dietary Fats and Atherosclerosis in Rat and Rabbit ... 169
Henson, J. B. and Crawford, T. B. (Pullman, Wash.) : The Pathogenesis of Virus-Induced
Arterial Disease - Aleutian Disease and Equine Viral Arteritis ............. 183
Hollander, W.; Colombo, M. A.; Kramsch, D. M., and Kirkpatrick, B. (Boston,
Mass.) : Immunological Aspects of Atherosclerosis (with 2 color plates) .... 192

IV. Spontaneous Congenital Heart Disease

Patterson, D. F. (Philadelphia, Pa.): Pathologic and Genetic Studies of Congenital
Heart Disease in the Dog ...................................................... 210
Laird, C. W. (Cambridge, Mass.): Developmental Electrocardiography in Inbred
Perinatal Hamsters .................................................................. 250
Sordahl, L. A. (Galveston, Tex.): Neonatal Cardiac Energetics: Relationship of
Physiologic Growth to Pathologic Growth .................................. 270
Dhalla, N. S.; Sulakhe, P. V.; Fedele, J. M., and Yates, J. C.: Molecular
Abnormalities in Cardiomyopathy ............................................. 282

V. Drug-Induced Myopathies and Related Subjects

Vatner, S. F. and Patrick, T. A. (Boston, Mass.): Instrumented Primates as
Cardiovascular Models......................................................... 302
Davies, R. O. (Montreal): β-Blockers in the Management of Myocardial Ischemia 315
Buja, L. M.; Ferrans, V. J., and Roberts, W. C. (Bethesda, Md.): Drug-Induced
Cardiomyopathies ................................................................ 330
Roberts, W. C.; Ferrans, V. J., and Buja, L. M. (Bethesda, Md.): Pathologic Aspects
of the Idiopathic Cardiomyopathies ........................................ 349
Index vols. 1-12 ..................................................................... 368

List of Contributing Authors

Abelmann, Walter H., MD, Heart Station, Boston City Hospital, Boston, MA 02118
(USA).
Buja, L. Maximilian, MD, Section of Pathology, National Heart and Lung Institute,
National Institutes of Health, Bethesda, MD 20014 (USA).
Bullock, B. C., DVM, The Arteriosclerosis Research Center and the Department of Comparative Medicine, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, N.C. 27103 (USA).

Colombo, M. A., Boston University Medical Center, Boston, MA 02118 (USA).

Crawford, T. B., College of Veterinary Medicine, Washington State University, Pullman, WA 99163 (USA).

Davies, R. O., MD, Department of Clinical Pharmacology, Ayerst Laboratories, Montreal (Canada).

Dhalla, N. S., Ph. D., Department of Physiology, Faculty of Medicine, University of Manitoba, 770 Bannatyne Avenue, Winnipeg, R3E OW3 (Canada).

Fedeleesova, Margaret, University of Manitoba, Winnipeg R3E OW3 (Canada).

Ferrans, Victor J., MD, Ph. D., Section of Pathology, National Heart and Lung Institute, National Institutes of Health, Bethesda, MD 20014 (USA).

Gainer, J. H., DVM, Bureau of Veterinary Medicine, Food and Drug Administration, Rockville, MD 20852 (USA).

Gorlin, R., Peter Bent Brigham Hospital, Boston, MA 02115 (USA).

Hadlow, W. J., DVM, Rocky Mountain Laboratory, Hamilton, MT 59840 (USA).

Harris, Leonard C., MD, Division of Pediatric Cardiology, The University of Texas Medical Branch, Galveston, TX 77550 (USA).

Henson, J. B., DVM, Ph. D., Department of Veterinary Pathology, College of Veterinary Medicine, Washington State University, Pullman, WA 99163 (USA).

Herman, M. V., MD, Cardiac Catheterization Laboratory, Peter Bent Brigham Hospital, Boston, MA 02115 (USA).

Hollander, W., MD, Section on Hypertension and Atherosclerosis, Division of Medicine, Boston University Medical Center, Boston, MA 02118 (USA).

Kramscher, M., Boston University Medical Center, Boston, MA 02118 (USA).

Kreulen, T. H., Peter Bent Brigham Hospital, Boston, MA 02115 (USA).

List of Contributing Authors VIII

Kirkpatrick, B., Boston University Medical Center, Boston, MA 02118 (USA).

Laird, C. W., Ph. D., 9 Bio-Research Institute, Commercial Avenue, Cambridge, MA 02141 (USA).

Luginbühl, H., MD, Institute of Animal Pathology, University of Bern, CH-3000 Bern (Switzerland).

McGill, H. C. jr., MD, Department of Pathology, The University of Texas Health Sciences Center, San Antonio, TX 78284 (USA).

Morrison, E. S., MD, Department of Pathology and Specialized Center of Research in Atherosclerosis, Albany Medical College, Albany, NY 12208 (USA).

Mott, G. E., Southwest Foundation for Research and Education, San Antonio, TX 78284 (USA).

Owens, .., Ph. D., Cardiovascular Division, Peter Bent Brigham Hospital, Boston, MA
Edel sei der Mensch, hülfreich und gut!

Denn das allein unterscheidet uns von allen Wesen die wir kennen.
Goethe, 1782

Let man be noble, generous and good!
For this alone distinguishes us from all the creatures which we know.

In an age where it seems that man turns more and more vulgar, callous and evil, men of good will search for ways to become more human and more humane. Is there a better way for scientists to do this than to engage in cooperative enterprises?
Introductory Remarks

F. Homburger

Alexander Pope has written, ‘Learn from the beasts the physic of the field’, and it has by now been widely accepted that progress in medicine comes not from clinical observation alone but from its combination with experimental medicine and biology. The most dramatic illustration of this concept is the strange combination of living things now circling the earth in the sky lab: men, guppies, spiders and single-cell organisms, all there to fathom the mysteries of gravity.

But interdisciplinary biomedical research calls for not only the simultaneous study of strange bed-fellows in terms of the beasts - it also requires the cooperation and cohabitation of often incompatible and usually eccentric human creatures, the investigators. While modern technology has solved the problem of creating a controlled environment wherein spiders, guppies and bugs can coexist with man, it has not yet devised a means of assuring the peaceful and productive coexistence of investigators from different fields and having different interests, and truly interdisciplinary and inter-institutional enterprise remains the exception rather than the rule in biomedical research.

This symposium is an effort to bring together investigators from many fields, Ph.D.s, veterinarians, MDs, and from many disciplines, internal medicine, physiology, biochemistry, biophysics, pathology, veterinary medicine and pathology, pharmacology, pediatrics, zoology, history of medicine1. In this

1 This is the fourth interdisciplinary symposium initiated by the Bio-Research Institute. The first one was on Man-Made Health Hazards in 1958, the second, on Carcinogenesis and Carcinogen Testing, 1967. The third was on the Pathology of the Syrian Hamster, 1970. Proceedings of the first symposium were not published. The second and third are volumes 11 and 16 of the series Progress in Experimental Tumor Research, Karger, Basel.

Homburger XI

it is a pioneering effort and its birth which we assist today has been preceded by arduous courtship, difficult conception and most complicated pregnancy. The concept of our symposium was first rejected by the American College of Cardiology which took from January 1971 to August 1971 to decide to refuse its support because this meeting was not attractive to college membership. We then tried other sources of support and were turned down by the National Foundation (February 1972), the Nuffield Foundation
(March 1972), the World Health Organization (March 1972), The Wellcome Trust (May 1972). Finally, the application submitted by the Massachusetts Heart Association to the National Institutes of Health June 1, 1972 was approved but not funded December 8, 1972.

During the period from December 1971 to April 1972 18 major drug houses and chemical manufacturers turned down our requests for support. It is because our advisory committee of Drs. Austen, Abelmann, Detweiler, Gertz, Jones, Robbins and Sonnenblick remained firm in its view that this was an important and useful enterprise and because of the perseverance of Mr. Irl Lucas, Executive Director of the Massachusetts Heart Association, that we are here today and have the privilege to participate in an exceptionally interesting symposium sponsored by the Bio-Research Institute and the Massachusetts Heart Association. It is a great pleasure to acknowledge the cooperation of the American Heart Association and its Council on Clinical Cardiology and the Academy of Veterinary Cardiology, who in this instance have displayed greater perception than their clinical brethren in human medicine. I also acknowledge with gratitude the contributions of S. Karger AG, the publisher of this symposium, and of Merck Sharp & Dohme, Pfizer, Inc., Hoffmann-La Roche and some anonymous contributors.

We are most indebted to the speakers who agreed to participate and to have their manuscripts ready for prompt publication. Only 9 out of 41 approached were unable to participate and one of these has submitted his manuscript in absentia.

It is difficult to understand why there are not more frequent concerted efforts of many disciplines to solve one of the many remaining problems of biomedical research, since the history of problem solving in this field is often one of successive steps taken by widely separated investigators in different disciplines. The events which led me to initiate a symposium on the heart may serve as illustration of how these things happen. Act one - as a pathologist at Yale I saw several hearts at autopsy, all with gross and histological signs of infarction, muscle necrosis, etc., but no demonstrable vascular occlusion.

Homburger XII

Later, as an experimental pathologist, I became aware of Selye’s work on metabolic cardiomyopathy. Our geneticists, Whitney and Nixon, developed a strain of Syrian hamsters with muscular dystrophy. I saw the heart of one of these in 1962, was reminded of my autopsy of 1942, and called Selye to recommend a man to study this new form of spontaneous cardiomyopathy; this brought the late Eörs Bajusz into the picture. If there had not been this meeting between the sensitized clinician and the geneticist
(who was not really interested in disease at that time), the development of our present knowledge on hereditary cardiomyopathy might have taken much longer.

Comparative experimental pathology of course has its place in science by itself, but, as a physician who turned experimental pathologist, I view it more as an important contributor to the solution of problems of human health preservation and disease prevention and treatment. It is notoriously difficult to translate or to extrapolate from beast to man and, in order that animal experiments be as relevant as possible, they must be planned as carefully as possible. Factors known to modify an experiment must be stringently controlled. Preferably, more than one species of animals must be used. The factors to be controlled include (but are not limited to) the nutritional, endocrine and genetic background of the animals. Much knowledge has been gained since the 1920s when inbred lines of mice were first developed and suggested as more reliable subjects than randombred animals. Yet, even today many of our clinical colleagues have little knowledge of the role of genetics in experimental pathology and some experimental pathologists still fail to recognize the fact that variability is unavoidable in random-bred animals and experimentation using these animals often is not reproducible. Genetic manipulation as simple as inbreeding has been used to produce various disease models in mice, hamsters and rabbits. The cardiomyopathy of the Syrian hamsters, first described by the staff of the Bio-Research Institute, has become a widely used tool in experimental cardiology.

We can look forward to a most fascinating three days and to an enlightening book on the comparative pathology of the heart. Cardiomyopathies, atheromatosis, congenital heart disease and induced myopathies will be reviewed as well as some related subjects. We shall learn about hamsters, swine, monkeys, pigeons, cats, dogs, rats and humans from babies to adults. I hope that many of you will be with us for all of the sessions even though they deal with a specialty other than your own, for the most important aspect of a symposium such as this is to broaden our horizons.