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PROGRESS IN CARDIOLOGY

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Edited by

PAUL N. YU, M.D.

Sarah McCort Ward Professor of Medicine and Head,
Cardiology Unit, University of
Rochester School of Medicine and Dentistry,
Rochester, New York

and

JOHN F. GOODWIN, M.D.

Professor of Clinical Cardiology,
Royal Postgraduate Medical School,
London, England

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SYMPOSIUM ON CORONARY CIRCULATION
(Chapters 1-6)

Guest Editor

FRANCIS J. KLOCKE, M.D.

Professor of Medicine and
Chief, Division of Cardiology
School of Medicine, State University of New York at Buffalo

PREFACE

The first six chapters in Volume 5 of *Progress in Cardiology* are devoted to a Symposium on Coronary Blood Flow. This Symposium, superbly organized by Dr. Francis J. Klocke, is intended to summarize current knowledge of coronary perfusion as it pertains to clinical cardiology.

In Chapter 1 Dr. Klocke and co-workers discuss the physiological principles which regulate flow in normal and abnormal states, emphasizing the pivotal importance of the "balance" between myocardial oxygen demand and supply. They also enumerate the essential elements of coronary microcirculation and various aspects of coronary collateral circulation.

Specific determinants of myocardial oxygen demand are considered by Drs. Parmley and Tyberg in Chapter 2. Studies of the isolated heart muscle and of intact heart have identified four major factors: heart rate, preload, after-load, and contractile state. The per cent of increase in myocardial oxygen demand is directly proportional to the per cent of increase in pressure work, heart rate or myocardial contractility, while it is much less with augmentation in volume work. The information included in this chapter is of appreciable interest to the clinician because his ability to reduce oxygen demand is often greater than his ability to augment oxygen supply, particularly in patients with coronary artery disease.

Chapter 3 deals with transmural variations in myocardial perfusion. While clinicians have long recognized the special vulnerability of the subendocardium to ischemia, our understanding of the fundamental processes governing supply-demand relationships within the myocardial wall has benefited enormously from the studies of Hoffman and colleagues using radioactive microspheres. The currently widespread application of microsphere techniques testifies to their value. Drs. Hoffman and Buckberg thoroughly review information pertinent to the coronary circulation in this chapter, which includes a discussion of regional myocardial oxygen needs, the

techniques of estimating regional myocardial blood flow and its various determinants, the importance and interpretation of phasic coronary blood flow patterns, and the methods of predicting subendocardial ischemia from the ratio of diastolic to sytolic pressure-time index.

In Chapter 4 Dr. Klocke summarizes the "state of the art" of a variety of measurements of myocardial flow in man, particularly as they apply to patients with coronary artery disease. Specific types of flow measurements are enumerated in an effort to minimize the confusion often associated with the interpretation of data now available in the literature. These include techniques for measuring: (1) average flow per unit weight for the left ventricle, (2) total flow for the entire left ventricle, (3) regional flow per unit weight within the left ventricle, and (4) flow through coronary artery bypass graft. Problems in methodology are addressed in detail since they too have contributed importantly to the confusion just mentioned.

Chapter 5 focuses on radioactive tracer techniques for evaluating coronary blood flow. Prepared by Dr. Maseri, it reflects the long-standing experience of Maseri, Donato and the Pisa group with a wide variety of radioactive techniques, including external counting, steady imaging, and dynamic regional recording. Pertinent aspects of isotopes, instrumentation, techniques and methodology are discussed in detail.

In Chapter 6, Drs. Strauss and Pitt survey the rapidly expanding field of myocardial perfusion imaging, point out the functions and limitations of the detection devices employed, and delineate the appearance of normal and abnormal scans. Several procedures in clinical use are (1) gated blood pool scan, (2) myocardial perfusion scan, and (3) invasive techniques for measurement of regional myocardial perfusion, i.e. intracoronary arterial injection of radioisotopes. At this stage, these approaches provide primarily qualitative information.

In Chapter 7 the left ventricular performance in cardiomyopathies is discussed by Dr. Besse. With videometric technique, the studies are facilitated by a semiautomatic detection system for assessing the left ventricular contour. Hypertrophic obstructive cardiomyopathy is characterized by an impairment of ventricular filling, whereas the primary disturbance in congestive and hypokinetic cardiomyopathies is markedly compromised myocardial contraction. The response to isoproterenol and beta-adrenergic blocking agent may serve as an important indicator of the advisability of surgical intervention for hypertrophic obstructive cardiomyopathy.

The recent advances in hemodynamic findings in patients with acute myocardial infarction are summarized by Dr. Rackley and associates in Chapter 8. They discuss the initial findings, serial changes, clinical correlation and prognosis of the disease based upon observations reported by them and other workers. They also examine the relationship between hemodynamic findings and noninvasive measurements. These observations undoubtedly provide an objective approach to optimal care and management in the early phase of acute myocardial infarction.

In Chapter 9 Dr. Sandler gives an informative and timely account of the cardiovascular responses encountered during recent space flight and ground-based studies and assesses the implications of these responses with respect to the health and well-being of the astronauts. He first describes the historical events of animal and human suborbital and orbital flights conducted in both the United States and the Soviet Union. He goes on to summarize the cardiovascular and electrolyte changes in the early stage of the space flight, continued observations on prolonged exposure to weightlessness, and major compensatory alterations in the immediate postflight period. The complex changes, which involve many systems in addition to the heart and blood vessels, include control of effective

blood volume, mechanoreceptor and vasomotor regulations, fluid and electrolyte balance, muscle and bone metabolism, manifestations of orthostatic instability and space sickness.

The electrocardiographic changes in digitalis intoxication are described by Dr. Wellens in Chapter 10. The following changes are highly suggestive: (1) bradycardia in patients previously showing normal or fast rates, (2) tachycardia in patients previously showing normal heart rates, (3) appearance of unexpected regularity in patients previously showing irregular rhythm, and (4) appearance of a rhythm characterized by a "regular" irregularity. It is emphasized that, if the arrhythmia presents a *change* from a previous rhythm in a patient receiving digitalis, it should be considered as evidence of digitalis intoxication until proven otherwise.

In Chapter 11 Drs. Kirkler and Curry present a comprehensive review of paroxysmal supraventricular tachycardias with new information derived from programmed elective stimulation applied to the intracardiac electrodes. Investigations are carried out to delineate refractory properties of the specialized tissues and myocardium, presence or absence of sino-atrial disease, anomalous atrioventricular connections, and the means to initiate and terminate arrhythmias. Two major types of supraventricular tachycardia are identified: (1) atrial tachyarrhythmias which include paroxysmal atrial tachycardia and atrial flutter and are primarily due to a focal or microreentry mechanism and (2) reciprocating tachycardias which develop as a consequence of reentry mechanisms, consisting of junctional reciprocating tachycardia, tachycardia associated with preexcitation syndrome and reciprocating sinus tachycardia.

Heart block, pacing, and pacemakers are reviewed by Dr. Harris in Chapter 12. The first section appraises the pathological changes of various types of heart block, including the heart block complicating acute myocardial infarction and chronic heart block observed in a number of disease entities. Chronic heart block may occur in idiopathic bilateral bundle branch block (Lev disease and Lenégre disease), coronary artery disease with old anteroseptal infarction, calcific aortic stenosis or mitral annulus, cardiomyopathies (idiopathic, amyloidosis, and hemochromatosis), familial skeletal myopathy, connective tissue disorders and other rare conditions. The second section of the chapter describes briefly the indications, techniques and beneficial effects of pacing. The final section discusses the use of pacemakers in chronic heart block, appended by a brief summary of various types of pacemakers and electrodes.

In Chapter 13 Dr. Pentecost gives a critical review of the success and deficiency of coronary care units (CCUs) in the United Kingdom. These are appraised from various viewpoints: (1) location and design, (2) nursing staff and physicians, (3) equipment and facilities, and (4) clinical management. He infers that while many CCUs in the United Kingdom are doing an excellent job, a number of them indeed have problems and deficiencies. For instance, a substantial number of CCUs are inadequately housed and staffed; in some of them monitoring equipment is unnecessarily complex and sophisticated; in others therapeutic measures used have not been validated scientifically or little progress in therapy has been achieved. The chapter is concluded with a brief discussion on the future extension of intensive care/mobile coronary care units.

It is our hope to continue to publish authoritative and timely reviews in *Progress in Cardiology*—which we believe has passed its test as a well-established annual series.

We wish to express our thanks and appreciation to Mrs. Summer King and Mrs. Sharon Pastwick for their assistance in handling the

manuscripts and proofs. Mrs. King has been very helpful to the editors for her liaison work with the contributors and publishers.

It has been a great pleasure for us to work with the excellent staff of Lea & Febiger. Mr. R. Kenneth Bussy, Mr. Francis C. Lea, Jr., Mr. Thomas Colaiezzi, Mrs. Rosemary Pattison and Mr. Lawrence Bentley have rendered us valuable service in making the publication of this series of *Progress in Cardiology* a real success.

Rochester, New York Paul N. Yu
London, England John G. Goodwin

CONTRIBUTORS

P. Besse, M.D.
Professeur Agrégé en Cardiologie
University of Bordeaux
Chief, Cardiovascular Laboratories
Centre de Cardiologie
Hôpital du Tondu
Bordeaux, France

Gerald D. Buckberg, M.D.
Associate Professor of Surgery
Division of Thoracic Surgery
Center for the Health Sciences
University of California, Los Angeles
Attending Surgeon
University of California Hospital
Los Angeles, California

Donald P. Copley, M.D.
Clinical Assistant Instructor in Medicine
State University of New York at Buffalo
Buffalo, New York

Paul V. L. Curry, M.B., M.R.C.P.
Assistant Lecturer in Cardiovascular Diseases
Royal Postgraduate Medical School
Honorary Senior Registrar
Hammersmith Hospital
London, England

Alan Harris, B.Sc., M.D., M.R.C.P.
Consultant Cardiologist
Charing Cross Hospital
London, England

Julien I.E. Hoffman, M.D., M.R.C.P.
Professor of Pediatrics
Senior Member, Cardiovascular Research Institute
University of California, San Francisco
Attending Pediatrician
Moffitt Hospital
San Francisco, California

Francis J. Klocke, M.D.
Professor of Medicine
Chief, Division of Cardiology
State University of New York at Buffalo
Attending Physician in Medicine
Chief of Cardiology
E. J. Meyer Memorial Hospital
Clinical Associate in Medicine
Buffalo General Hospital
Consultant
Buffalo Veterans Administration Hospital
Buffalo Psychiatric Center
Buffalo, New York

Dennis M. Krikler, M.D., F.R.C.P., F.A.C.C.
Lecturer in Cardiovascular Diseases
Royal Postgraduate Medical School
Consultant Cardiologist
Hammersmith and King Edward Hospitals
London, England

John A. Mantle, M.D.
Assistant Professor of Medicine
University of Alabama Medical Center
Birmingham, Alabama

Attilio Maseri, M.D.
Professor of Cardiopulmonary Pathophysiology
Postgraduate Medical School
University of Pisa
Head, Coronary Section
Clinical Physiology Laboratory of the National Research Council
Pisa, Italy

Robert E. Mates, Ph.D.
Professor of Mechanical Engineering
Research Associate Professor of Medicine
State University of New York at Buffalo
Buffalo, New York

Roger E. Moraski, M.D.
Physician in private practice
Birmingham, Alabama

Arthur E. Orlick, M.D.
Clinical Assistant Instructor in Medicine
State University of New York at Buffalo
Buffalo, New York

William W. Parmley, M.D.
Professor of Medicine
Cardiovascular Research Institute
University of California, San Francisco
Chief, Division of Cardiology
Moffit Hospital
San Francisco, California

B. L. Pentecost, M.D., F.R.C.P.
General Hospital
Birmingham, England

Bertram Pitt, M.D.
Associate Professor of Medicine
Johns Hopkins University School of Medicine
Baltimore, Maryland

Charles E. Rackley, M.D.
Professor of Medicine
Director, Specialized Center of Research for Ischemic Heart Disease
University of Alabama Medical Center
Birmingham, Alabama

Richard O. Russell, Jr., M.D.
Professor of Medicine
University of Alabama Medical Center
Birmingham, Alabama

Harold Sandler, M.D.
Associate Clinical Professor of Medicine
Stanford University School of Medicine
Palo Alto, California
Chief, Biomedical Research Division
NASA-Ames Research Center
Moffett Field, California

H. William Strauss, M.D.
Associate Professor of Radiology and Nuclear Medicine
Johns Hopkins University School of Medicine
Baltimore, Maryland

John V. Tyberg, M.D., Ph.D.
Assistant Professor of Medicine and Physiology
Associate Staff Member, Cardiovascular Research Institute
University of California, San Francisco
San Francisco, California

Hein J. J. Wellens, M.D.
Professor of Cardiology
University of Amsterdam
Amsterdam, The Netherlands

CONTENTS

Chapter 1

PHYSIOLOGY OF THE CORONARY CIRCULATION IN HEALTH AND CORONARY ARTERY DISEASE*

Francis J. Klocke, M.D., Robert E. Mates, Ph.D., Donald P. Copley, M.D., and Arthur E. Orlick, M.D.

RELATIONSHIP BETWEEN MYOCARDIAL OXYGEN DEMAND AND SUPPLY

Since the primary function of the coronary circulation is to supply the heart's metabolic needs, any discussion of the physiology of the coronary circulation must begin by emphasizing the unusually close linkage between myocardial metabolism and perfusion. This relationship is illustrated schematically in Figure 1. The left-hand side of the balance represents myocardial metabolic demand. Since the heart has a limited and short-lived capacity for anaerobic metabolism, its metabolic needs can be considered solely in terms of oxidative metabolism. $M\dot{V}O_2$ represents the total oxygen uptake required to satisfy the needs imposed by the various determinants of oxygen demand. The right-hand side of the balance represents myocardial oxygen supply, which can be expressed as the product of coronary flow and the coronary arteriovenous oxygen difference. One of the unique features of the coronary circulation is its high degree of oxygen extraction under basal conditions. Coronary venous oxygen saturation is typically only 20 to 30 per cent, making it difficult for the heart to adjust to

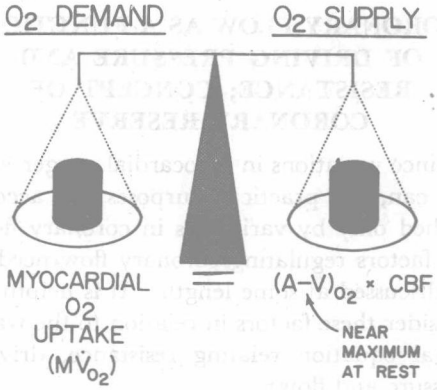

Fig. 1. Schematic representation of the normal balance between myocardial oxygen demand and supply. $(A\text{-}V)_{O_2}$ = arteriovenous oxygen difference; CBF = coronary blood flow.

* Supported by Program-Project Grant HL-15194 from the National Heart and Lung Institute, National Institutes of Health, Bethesda, Maryland.

changing metabolic needs by an increased extraction of oxygen from incoming arterial blood. Accordingly, changes in $M\dot{V}O_2$ mandate changes in coronary flow which are directionally similar and equal in magnitude. Because of this relationship between $M\dot{V}O_2$ and flow, it is apparent that the "normality" or "abnormality" of an individual value of flow can be evaluated only in light of the coexistent oxygen demand.

The various determinants of myocardial oxygen demand are discussed in detail by Drs. Parmley and Tyberg in Chapter 2. Of particular importance are wall stress, contractile state and heart rate (insofar as changes in rate alter the total amount of stress generated in a given time interval). While it is often possible to predict directional changes in $M\dot{V}O_2$ from hemodynamic measurements, quantitative estimates of changes in $M\dot{V}O_2$ are extremely difficult. In coronary artery disease, there is the special problem of dealing with changes in oxygen demand in localized regions within the left ventricle. In addition, as discussed subsequently in this chapter and in Chapter 3 by Drs. Hoffman and Buckberg, it seems likely that transmural variations in oxygen demand occur in both normal and abnormal hearts. Thus, future studies aimed at an improved quantitative definition of $M\dot{V}O_2$ are of great interest.

CORONARY FLOW AS A FUNCTION OF DRIVING PRESSURE AND RESISTANCE; CONCEPT OF CORONARY RESERVE

Since variations in myocardial oxygen supply can, for practical purposes, be accomplished only by variations in coronary flow, the factors regulating coronary flow need to be discussed at some length. It is helpful to consider these factors in relation to the traditional equation relating resistance, driving pressure and flow:

$$\dot{Q} = \frac{\Delta P}{R} \qquad (1)$$

where: $\dot{Q}$ = coronary flow, ΔP = driving pressure across the coronary vascular bed (this is usually considered to be the difference between input and output pressures, i.e. between aortic and right atrial pressures. However, because of the small and reasonably constant magnitude of right atrial pressure, ΔP is often approximated by aortic pressure alone), and R = total coronary resistance.

This straightforward representation of the pressure-flow relationships within the coronary circulation involves assumptions the validity of which has been difficult to assess directly. Of particular importance is the implication that the impedance to flow offered by the coronary vascular bed is purely resistive in nature. In reality, the impedance also contains inertial and elastic components, i.e. the total system should be viewed as the hydraulic equivalent of an electrical circuit containing inductors and capacitors as well as resistors. Inertial effects are confined primarily to the larger arteries where velocities are significant, while capacitive effects relate to blood vessel elasticity. Most investigators have felt that the inductive and capacitive components of impedance are normally of minor importance. This impression has recently been substantiated by Gupta,[55] who performed Fourier analyses on a variety of published records of simultaneous central aortic pressure and coronary flow. Since the magnitude of calculated impedance was independent of frequency, Gupta concluded that a purely resistive model is adequate to describe input impedance in hearts generating normal arterial pressures at normal heart rates. Although nonresistive components of impedance could theoretically become significant under other conditions, e.g. higher heart rates or elevated aortic pressures, these components will not be considered further in this discussion.

Application of equation 1 to normal physiological states requires detailed consideration of the various factors involved in the resistive component of impedance. It is useful to model total coronary resistance as the sum of