Clinical Cardiology

Edited by

James T. Willerson Charles A. Sanders

Clinical Cardiology

Edited by

James T. Willerson, M.D., F.A.C.C.

Professor of Medicine
and Director, Ischemic Heart Center
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

Charles A. Sanders, M.D., F.A.C.P., F.A.C.C.

Associate Professor of Medicine
Harvard Medical School
and General Director and Physician
Massachusetts General Hospital
Boston, Massachusetts

GRUNE & STRATTON
A Subsidiary of Harcourt Brace Jovanovich, Publishers
New York San Francisco London

Volume III of
THE SCIENCE AND PRACTICE OF CLINICAL MEDICINE

Jay P. Sanford, M.D.
Editor-in-Chief
Professor of Internal Medicine
and Dean, School of Medicine
Uniformed Services University of the Health Sciences
Bethesda, Maryland

Library of Congress Cataloging in Publication Data
Main entry under title:
Clinical cardiology.
(The Science and practice of clinical medicine; v. 3)
Includes bibliographies and index.
1. Cardiology. I. Willerson, James T. II. Sanders, Charles A. III. Series. [DNLM: 1. Cardiovascular diseases. WG100 C6405]
RC681.C66 616.1'2 77-1449
ISBN 0-8089-0992-4

Grune & Stratton, Inc.
111 Fifth Avenue
New York, New York 10003

Distributed in the United Kingdom by
Academic Press, Inc. (London) Ltd.
24/48 Oval Road, London NW 1

Library of Congress Catalog Number 77-1449
International Standard Book Number 0-8089-0992-4
Printed in the United States of America

Acknowledgments

The Editors wish to express their appreciation to the contributing authors for their efforts in preparing and delivering their discussions and for their patience and understanding in meeting the necessary deadlines for the topics they were invited to submit. The Editors would also like to acknowledge the constructive criticism and suggestions of many colleagues and express their gratitude to their secretaries, Mrs. Belinda Lambert, Ms. Donna Place, and Ms. Irene Calk, for excellent secretarial assistance. Finally, they wish to thank the publishers for their skilled technical help.

Preface

As we undertook the writing of *Clinical Cardiology* we wished to develop a textbook that would be a working manual of adult clinical cardiology. Our aim was not to be encyclopedic in coverage but rather to provide detailed, but relevant, discussions of subjects pertinent to the management of adult patients with heart disease in the mid and late 1970s. We were especially anxious to provide a firm physiologic foundation for each important area of clinical cardiology with the expectation that this foundation might allow one to predict or correctly surmise that which might not yet be well understood and to correctly apply or further develop accepted medical principles as they apply to the care of patients with heart disease.

We hope that this approach to the problems of clinical cardiology will provide the student, house officer, and practicing physician with a useful textbook of clinical cardiology.

James T. Willerson, M.D., F.A.C.C.
Charles A. Sanders, M.D., F.A.C.P., F.A.C.C.

Contributors

Paul W. Armstong, M.D.
Associate Professor of Medicine
Queen's University
and Director, Coronary Care Unit
Kingston General Hospital
Kingston, Ontario, Canada

James M. Atkins, M.D.
Assistant Professor of Medicine
Cardiopulmonary Division
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

Henry R. Besch, Ph.D., F.A.C.C.
Associate Professor of Pharmacology and Medicine
and of Medical Biophysics
Indiana University School of Medicine
Indianapolis, Indiana

J. Thomas Bigger, Jr., M.D.
Professor of Medicine and of Pharmacology
College of Physicians and Surgeons
Columbia University
New York, New York

David W. Bilheimer, M.D.
Assistant Professor of Medicine
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

Margaret B. Billingham, M.D.
Assistant Professor of Pathology
Stanford University School of Medicine
and Stanford University Hospital
Stanford, California

C. Gunnar Blomqvist, M.D., Ph.D.
Professor of Medicine and Physiology
Cardiopulmonary Division
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

Frederick J. Bonte, M.D.
Dean, Southwestern Medical School
The University of Texas Health Science Center at Dallas
Dallas, Texas

L. Maximilian Buja, M.D.
Assistant Professor of Pathology
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

James B. Caulfield, M.D.
Chairman, Department of Pathology
Division of Health Affairs
University of South Carolina
Columbia, South Carolina

Ernest Craige, M.D.
Chief of Cardiology
North Carolina Memorial Hospital
and Henry A. Foscue Distinguished Professor of
Cardiology
University of North Carolina School of Medicine
Chapel Hill, North Carolina

Robert E. Dinsmore, M.D.
Associate Professor of Radiology
Harvard Medical School
and Radiologist
Massachusetts General Hospital
Boston, Massachusetts

David E. Fixler, M.D.
Associate Professor of Pediatrics
The University of Texas Health Science Center at Dallas
Southwestern Medical School
and Director of Cardiology
Childrens Medical Center
Dallas, Texas

John T. Flaherty, M.D.
Assistant Professor of Medicine
Cardiology Division
Johns Hopkins University School of Medicine
Johns Hopkins Hospital
Baltimore, Maryland

Charles K. Francis, M.D.
Chief of Cardiology
Martin Luther King Medical Center
Los Angeles, California

Herman Gold, M.D.
Assistant Professor of Medicine
Harvard Medical School
and Assistant in Medicine
Cardiac Unit
Massachusetts General Hospital
Boston, Massachusetts

Allan Goldblatt, M.D.
Associate Professor of Pediatrics
Harvard Medical School
and Pediatrician and Chief
Pediatric Cardiology Unit
Massachusetts General Hospital
Boston, Massachusetts

William Grossman, M.D.
Associate Professor of Medicine
Harvard Medical School
and Director, Cardiac Catheterization Laboratories
Peter Bent Brigham Hospital
Boston, Massachusetts

M. Dean Harris, M.D.
Assistant Professor of Internal Medicine
Cardiopulmonary Division
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

Donald C. Harrison, M.D.
Professor of Medicine
Stanford University School of Medicine
and Chief, Cardiology Division
Stanford University Hospital
Stanford, California

J. Warren Harthorne, M.D., F.A.C.P., F.A.C.C.
Assistant Professor of Medicine
Harvard Medical School
and Associate Physician
Cardiac Unit
Massachusetts General Hospital
Boston, Massachusetts

L. David Hillis, M.D.
Cardiac Unit
Peter Bent Brigham Hospital
Boston, Massachusetts

Sharon A. Hunt, M.D.
Postdoctoral Fellow in Cardiology
Stanford University Hospital
Stanford, California

Harry R. Jacobson, M.D.
Major, MC
and Chief, Renal Section
Army Institute of Surgical Research
Brooke Army Medical Center
Fort Sam Houston
San Antonio, Texas

Robert L. Johnson, M.D.
Professor of Internal Medicine
Cardiopulmonary Division
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

Jan Koch-Weser, M.D.
Director, Centre de Recherche Merrell International
Strasbourg, France

Juha P. Kokko, M.D., Ph.D.
Chief of Nephrology
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

Nolan J. Laborde, Jr., M.D.
Cardiology Fellow
University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

Kirk M. Lipscomb, M.D.
Department of Internal Medicine
The University of Texas Health Science Center at Dallas
Southwestern Medical School
and Cardiovascular Section
Veterans Administration Hospital
Dallas, Texas

James P. Luby, M.D.
Associate Professor of Internal Medicine
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

Jay W. Mason, M.D.
Assistant Professor of Medicine
Cardiology Division
Stanford University School of Medicine
Stanford University Hospital
Stanford, California

John A. Mills, M.D.
Associate Professor of Medicine
Harvard Medical School
and Arthritis Unit
Massachusetts General Hospital
Boston, Massachusetts

Lawrence J. Mills, M.D.
Assistant Professor of Thoracic and Cardiovascular Surgery
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

Jere H. Mitchell, M.D.
Professor of Internal Medicine and Physiology
Cardiopulmonary Division
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

Gilbert S. Omenn, M.D., Ph.D.
Associate Professor of Medicine
University of Washington
and Investigator
Howard Hughes Medical Institute
Seattle, Washington

Suzanne Oparil, M.D.
Associate Professor of Medicine
Pritzker School of Medicine
University of Chicago
Chicago, Illinois

Robert W. Parkey, M.D.
Chief, Nuclear Medicine
Department of Radiology
Parkland Memorial Hospital
and The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

Somsong Penpargkul, M.D., Ph.D.
Assistant Professor of Medicine
Albert Einstein College of Medicine
and Division of Cardiology
Montefiore Hospital and Medical Center
Bronx, New York

Joseph K. Perloff, M.D.
Professor of Medicine and Pediatrics
and Chief, Cardiovascular Section
University of Pennsylvania School of Medicine
Philadelphia, Pennsylvania

Melvin R. Platt, M.D.
Assistant Professor
and Chairman, Thoracic and Cardiovascular Surgery
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

Gerald M. Pohost, M.D.
Instructor in Medicine
Harvard Medical School
and Cardiac Unit
Massachusetts General Hospital
Boston, Massachusetts

Lawrence R. Poliner, M.D.
Assistant Professor of Internal Medicine
Cardiopulmonary Division
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

William John Powell, Jr., M.D.
Associate Professor of Medicine
Harvard Medical School
and Assistant Physician
Massachusetts General Hospital
Boston, Massachusetts

Alan K. Rider, M.D.
Redwood Medical Clinic
Redwood City, California

William S. Ritter, M.D.
Chief of Cardiology
Reynolds Army Hospital
Fort Sill, Oklahoma

Charles R. Rosenfeld, M.D.
Assistant Professor of Pediatrics and Obstetrics-Gynecology
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

James Scheuer, M.D.
Professor of Medicine
Albert Einstein College of Medicine
and Director, Division of Cardiology
Montefiore Hospital and Medical Center
Bronx, New York

Kenneth I. Shine, M.D.
Chief, Division of Cardiology
The Center for Health Sciences
University of California at Los Angeles
Los Angeles, California

J. Donald Smiley, M.D.
Professor of Internal Medicine
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

Thomas W. Smith, M.D.
Associate Professor of Medicine
Harvard Medical School
and Chief, Cardiovascular Division
Peter Bent Brigham Hospital
Boston, Massachusetts

Thomas C. Smitherman, M.D.
Assistant Professor of Internal Medicine
The University of Texas Health Science Center at Dallas
Southwestern Medical School
and Cardiovascular Section
Veterans Administration Hospital
Dallas, Texas

Richard D. Spangler, M.D.
Departments of Medicine and Radiology
University of Colorado Medical Center
and Director, Cardiovascular Laboratory and Non-Invasive Laboratory
St. Anthony Hospital
Denver, Colorado

Edward B. Stinson, M.D.
Associate Professor of Cardiovascular Surgery
Stanford University School of Medicine
Stanford, California

Jan P. Szidon, M.D.
Chief, Pulmonary Medicine Division
Michael Reese Hospital and Medical Center
Chicago, Illinois

Richard L. Taw, M.D.
Director, Non-Invasive Laboratories
Division of Cardiology
The Center for Health Sciences
University of California at Los Angeles
Los Angeles, California

Ralph Tompsett, M.D.
Professor of Medicine
The University of Texas Health Science Center at Dallas
Southwestern Medical School
and Baylor University Medical Center
Dallas, Texas

August M. Watanabe, M.D.
Associate Professor of Medicine and Pharmacology
Krannert Institute of Cardiology
Indiana University School of Medicine
Indianapolis, Indiana

Myron L. Weisfeldt, M.D.
Director, Cardiology Division
Johns Hopkins University School of Medicine
Johns Hopkins Hospital
Baltimore, Maryland

James E. Wilson, III, M.D.
Associate Professor of Medicine
Cardiopulmonary Division
The University of Texas Health Science Center at Dallas
Southwestern Medical School
Dallas, Texas

Douglas P. Zipes, M.D., F.A.C.P., F.A.C.C.
Professor of Medicine
and Director of Cardiovascular Research
Krannert Institute of Cardiology
Indiana University School of Medicine
Indianapolis, Indiana

Contents

ANATOMY OF THE CARDIOVASCULAR SYSTEM

James B. Caulfield

The heart and the blood vessels form a continuous conduit system for circulation of the blood, with the heart providing the force. The system is capable of a wide range of performance, in toto and regionally; i.e., the cardiac output can vary under physiologic loads from 3 to 30 liters per minute, and local blood flow to a stimulated muscle or to the skin may vary by 200 percent or more. This wide range in function occurs with little loss in efficiency. The form of the heart and the blood vessels provides a partial basis for this range of activity. Control of the system's potential is vitally necessary and is provided by an extensive network of sensing organs that deliver a constant flow of information to central integrative nuclei in the brain stem. These nuclei activate appropriate effector organs through extensive ramifications of sympathetic and parasympathetic nerve plexuses. The following description of the cardiovascular system is by no means complete. Rather, the aspects most easily related to its functioning in normal and abnormal states are covered, but the references should be consulted for more complete exposition in most cases.

GROSS ANATOMY OF THE HEART

The heart is enveloped by the pericardial sac, a derivative of the embryonic dorsal mesocardium. The heart in its earliest developmental stages is a straight tube surrounded by the mesocardium, with venous and arterial sides of the circulation at either end of this straight tube. As the heart undergoes its various convolutions the initial simple pericardial-heart relationships become more complex. The result is a sac with a reflection that invests the aorta and pulmonary artery and a second reflection investing the two caval and four pulmonary veins. At these reflection points the pericardial sac is continuous with the epicardial connective tissue forming the visceral pericardium.

The pericardial sac is composed of interwoven bands of collagen resulting in a tough sac that can be stretched only very slowly. The surface facing the heart is lined by mesothelial cells, as is the epicardial surface of the heart. These cells contribute to the pericardial fluid that presumably provides a lubricated surface for the constantly moving heart. The pericardial sac is tightly adherent to the central tendon of the diaphragm and more loosely attached to the upper and lower ends of the sternum by the sternopericardial ligaments.

The pericardial sac or parietal pericardium is innervated by a branch of the phrenic nerve which contains pain fibers. However, the visceral pericardium does not receive branches of the phrenic and is insensitive to pain stimuli.

The heart can be oriented within the thorax by utilizing various planes defined by its intrinsic structure and referring these planes to fixed thoracic structures (Fig. 1). The plane defined by the interatrial and interventricular septa forms an angle of 41°-45°, with a vertical plane bisecting the sternum and vertebral column. Since this plane roughly defines the ventricular inflow and outflow tracts, blood flows at a 45° angle from the median of both atria to both ventricles and out the pulmonary and aortic vessels at this same orientation. The fibrous ring of the mitral and tricuspid valves forms a plane dividing the ventricles and atria and is approximately 45° from vertical and 80° from horizontal. These planes indicate that the right atrium and ventricle are below and anterior to the left atrium and ventricle and that the blood flow from the atria to the ventricles follows a line 45° from the median toward the left and has about a 10° downward inclination as viewed from an anterior position. This particular orientation is somewhat difficult to work with because of the overlap of the atria and ventricles; oblique views provide sharper delineation of the various heart chambers. The external relationships of the heart are quite important and are dealt with in detail in standard anatomy textbooks.

Mammalian hearts are divided into atria and ventricles by a fibrous ring from which all the muscle bundles arise and insert and into which the atrioventricular valves insert. The atria and ventricles are divided into right and left portions by septa. This left-right relationship is true in embryonic life, but by 4½ months the previously described adult overlap situation is attained.

All the muscle fibers of the heart arise and insert into the centrally located fibrous structure, thus forming a continuous loop. The atria have two indistinct layers of muscle: a superficial and a deep. The superficial fibers arise from the atrioventricular rings and either encircle both atria or turn in at the interventricular septum, course

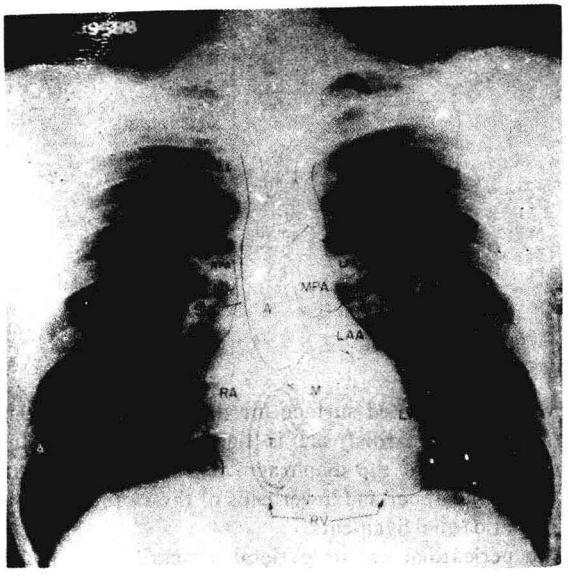

Fig. 1. An x-ray of the chest with some cardiovascular landmarks indicated: RPA, right pulmonary artery; SVC, superior vena cava; RA, right atrium; A, aorta; T, tricuspid valve ring; MPA, main pulmonary artery; M, mitral valve ring; RV, right ventricle; LPA, left pulmonary artery; LAA, left auricular appendage; LV, left ventricle.

through, and loop around the opposite atrium to form a figure eight. The deeper atrial fibers originate at one atrioventricular ring and course through the wall of one atrium to insert in the fibrous ring of the atrioventricular valve.

The disposition of fibers in the two ventricles is similar, the major difference being a marked thickening of the central encircling fibers of the left ventricle (Fig. 2). Individual heart cells are characterized by branching processes. These processes extend both laterally and to a deeper layer of muscle. With such a branching system, no clear-cut fascial planes or lines of separation are present. The ventricular myocardium consists of one muscle mass

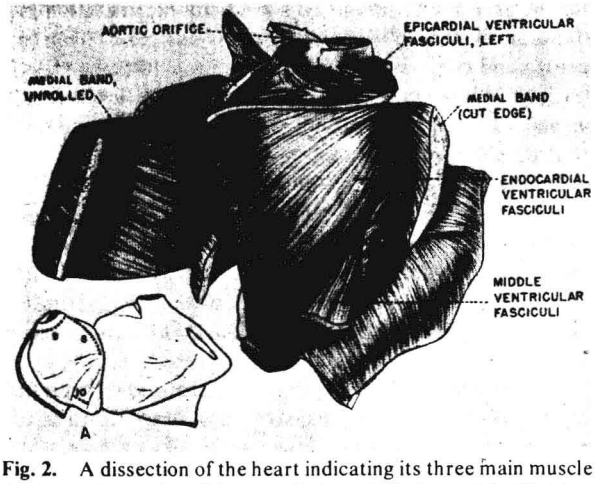

Fig. 2. A dissection of the heart indicating its three main muscle fascicles. (Reproduced by permission of M. Lev, C.S. Simkins, Lab Invest 5:396, 1956)

with numerous cross branches to adjacent fibers. The fibers in any given location extend in approximately the same direction. The superficial muscle fibers consisting of the outer 1–2 millimeters (mm) of the ventricle arise from the fibrous skeleton at the base of the heart and, as viewed from the apex, course toward it in a soft, helical, clockwise spiral. Throughout the downward sweep the superficial fibers, by branching processes, dip into the central portion, at which time they bend sharply clockwise to become circumferentially oriented to the long axis of the heart and form the bulk of the left ventricle but only a small portion of the right ventricle.

At the apex the superficial fibers dip into the myocardium, forming a vortex. These fibers continue toward the base in a helical spiral oriented about 90° to the superficial layer. These subendocardial fibers form the papillary muscles which are inserted in the central valve ring via the chordae tendineae and atrioventricular valves. The remaining subendocardial fibers insert into the central fibrous skeleton. Thus the form of the heart is that of a continuous muscle bundle created by individual cells that branch.

The heart is essentially a cylindrical displacement-type pump and as such requires valves for unidirectional flow. The venous return to the atria both systemic and pulmonary is not anatomically valved in adults. Therefore, during atrial contraction there is some backflow, but most of the ventricular filling takes place during atrial diastole, and the final increment resulting from atrial contraction is not hampered by the absence of backflow valves. However, in the absence of good atrial function, cardiac efficiency is decreased and although valving at the atrial inflow is not necessary, organized atrial contraction is.

Both ventricles function at considerably higher pressure than the atria, and incompetent atrioventricular valves put a severe strain on the heart. The right atrioventricular valve (tricuspid) arises from the atrioventricular ring as three delicate leaflets with a complete endothelial covering overlying a spongiosa of collagen and elastic tissue (Fig. 3). The central body of the valve between the two spongiosa layers is of well-organized collagen. These three layers continue from the undersurface and margin of the valve as round chordae tendineae to insert into the papillary muscles. The left atrioventricular valve (mitral) is similar but consists of two cusps, the larger anterior medial and the smaller posterior lateral (Fig. 4). Chordae from each leaflet insert into both anterior and posterior papillary muscles. Closing of these valves is an integrated process involving atrial and ventricular contraction. During diastole the valve leaflets tend to float in the passing bloodstream, offering no resistance. Atrial contraction forces blood into the ventricle and causes the leaflets to float toward the atrium with a decrease in the size of the orifice. Contraction of the papillary muscles early in the ventricular systole following atrial systole and rising intraventricular pressure force and hold the contact margins of the leaflets together, forming a competent valve at the two atrioventricular orifices.

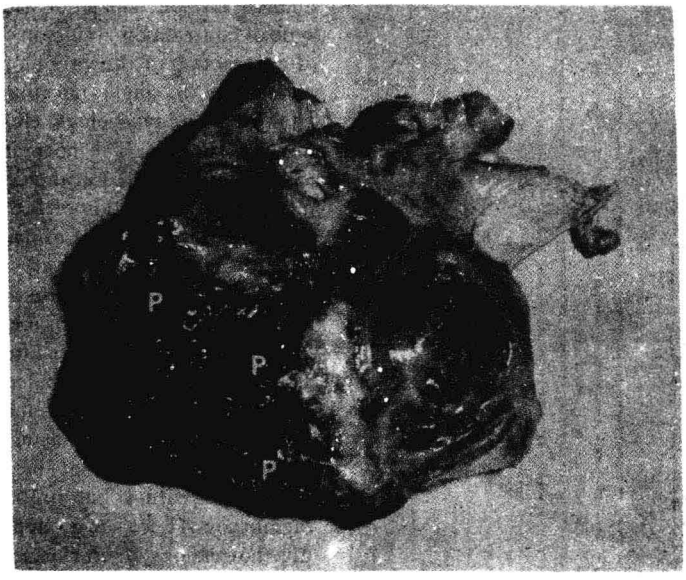

Fig. 3. Tricuspid valve. The right ventricle has been opened at the acute margin. The three small papillary muscles (P) are indicated. Crossover of chordae to more than one leaflet is not as extensive as is seen in the mitral complex. The outflow tract is at a 45 degree angle up from the central P.

The pulmonic and aortic valves are similar and are composed of three delicate semilunar leaflets of fibrous connective tissue with an endothelial covering (Fig. 5). The concavity of these valves faces the large vessel, and during diastole the backflow in the large vessel forces the margins of the three leaflets sufficiently close together to prevent regurgitation into the ventricle. These leaflets are delicate and quite pliable and as intraventricular pressure rises above pulmonic or aortic pressure they are easily moved upward and laterally. Like the atrioventricular leaflets, these valves tend to float in the bloodstream rather than appose the vessel wall closely. The two main coronary arteries arise from the aortic sinuses at a point slightly below the upper insertion of the semilunar valves

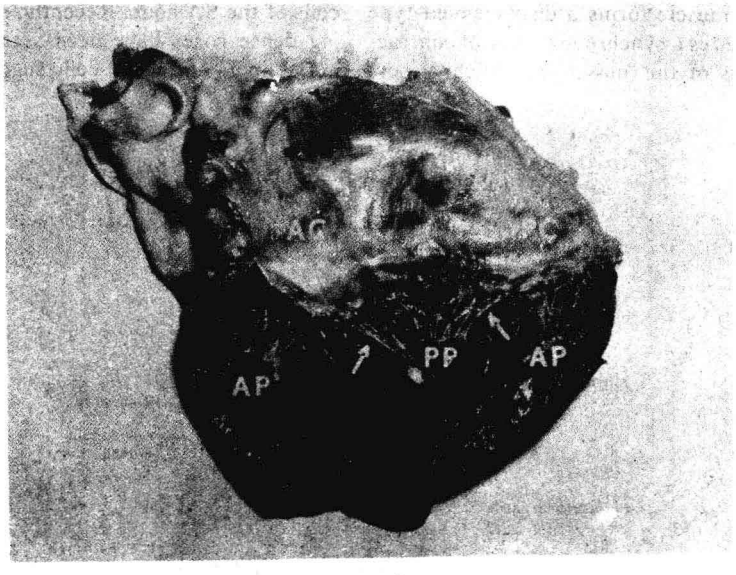

Fig. 4. Opened left ventricle displaying the mitral valve. The anterior papillary muscle (AP) has been bisected with half at either margin of the picture. Both the anterior papillary muscle and the posterior papillary muscle (PP) contribute chordae (arrows) to both the anterior leaflet (AC) and posterior leaflet (PC) of the mitral valve. In this case the posterior papillary muscle is partially split with two separate heads but a single base.

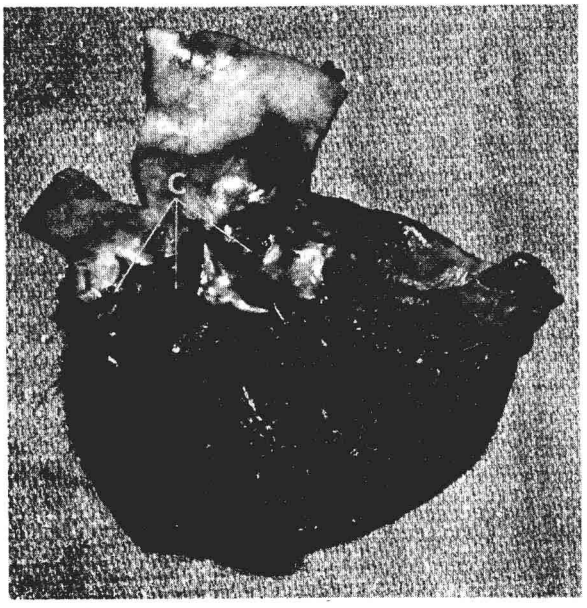

Fig. 5. Aortic valve. The three cusps of the aortic valve are indicated. The left cusp from which the left coronary artery arises has been bisected, and half appears at either side of the aorta. The central line indicates the right cusp from which the right coronary artery originates, and the line to the right indicates the posterior cusp.

and opposite the midpoint of the valve. This location in the aortic sinus is well positioned to provide coronary flow during diastolic closing of the aortic valves.

ANATOMY OF THE CONDUCTION SYSTEM

The single heart muscle forms a displacement-type pump and as such requires a synchronous type of contraction of various regions of this muscle in a highly coordinated fashion. Deviation from the normal coordinated type of contraction results in decreased efficiency. Timing of contraction of the various parts of the heart is accomplished by a single pacemaker with specialized morphological and physiologic elements for distribution of the impulse (Fig. 6). The normal pacemaker, the sinoatrial (SA) node, is located at the cephalic end of the sulcus terminalis at the junction of the superior vena cava and the atrium. From this point of origin of the impulse, it is carried to all points of the atria by the atrial muscle cells themselves. Within the atria there are a number of regions in which the transmembrane action potential is distinct from that of the usual atrial fibers. These areas define specialized cells for both impulse generation and differential conduction velocity. The impulse generating cells are characterized by spontaneous depolarization. This spontaneous activity cannot be recognized by any unique structural feature but probably resides in the plasma membrane. There are groups of cells within the atria with the morphology of Purkinje cells, as well as the transitional forms between Purkinje and cardiac myocytes. These cells have a high rate of impulse conduction, and three bundles of such cells connecting the SA node with the atrioventricular (AV) node have been described. There are dense bundles of connective tissue surrounding the cells of the SA node. These dense bundles are thought to be part of the diffusion barrier that makes the cells of the SA node much less sensitive to large changes in the concentration of ionic potassium. The region of the SA node is richly supplied with nerve endings that arise from the vagus and the three cervical ganglia, principally the stellate ganglion, and modify the rate of impulse generation of the SA node. The nerves do not terminate on the cells of the SA node. Recently, synaptic vesicles containing dense cores have been seen in the matrix between nerve fibers and nodal cells suggesting that nervous con-

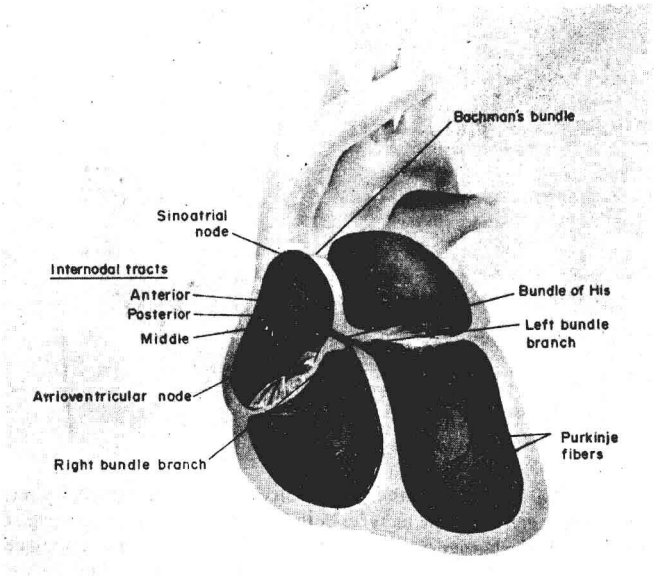

Fig. 6. Diagrammatic representation of the impulse generating and conducting systems of the human heart.

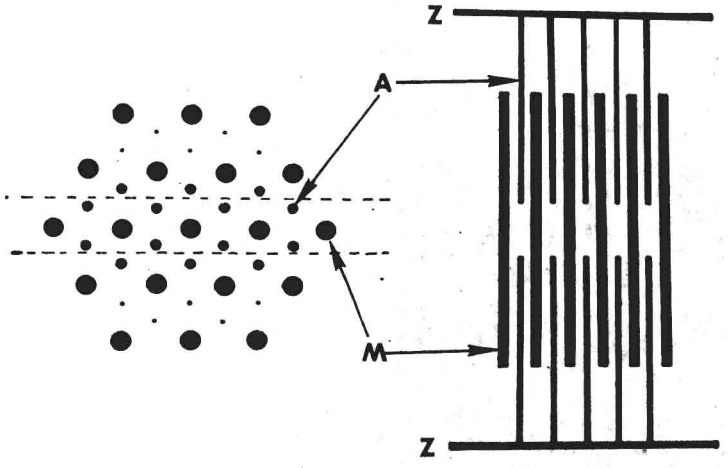

Fig. 7. Schematic of the relationship of actin (A) to myosin (M). The basic contractile unit, the sarcomere, consists of the elements between two Z bands. (Reproduced by permission of H. E. Huxley, J Biophys Biochem Cytol 3:631, 1957).

trol of this region occurs by release of neurohumoral agents that modify the milieu rather than by direct synaptic transmission. The sinoatrial impulse spreads concentrically from its point of origin via the atrial muscles. Upon reaching the Purkinje-type fibers that are present in various areas, impulse propagation rate is increased and the impulse is differentially distributed. The three anatomically defined bundles from the SA node carry the impulse to the AV node or "AV junctional region." This group of cells is located in the interatrial septum, posteriorly, close to the entrance of the coronary sinus. Impulse conduction is very slow in this area, resulting in a delay of ventricular activation. The impulse outflow of this region is conducted anteriorly via a group of specialized conducting cells, the Purkinje cells. This bundle descends toward the ventricles and divides into two bundles, a left and a right, which then ramify over the endocardium of the respective ventricles from the septal region downward and up the lateral walls of the ventricles. The subendocardial impulse is conducted via these specialized fibers with a high rate of impulse conduction, but from the subendocardial region to the epicardial surface and through the septum it passes from muscle cell to muscle cell at a slower rate.

The result of this complex conduction system is sequential stimulation of the contractile elements of the heart in a coordinated fashion. This creates physiologically definable areas of motion during cardiac contraction, such as the initial motion and shortening of the long axis of the heart with increase in the short diameter, creating a chamber closer to a sphere. This differential contraction more truly represents the muscle bundles of the heart rather than indistinct anatomic planes resulting from dissection.

STRUCTURE OF THE HEART CELLS

The geometric changes in the heart result from conversion of chemical energy to mechanical energy. This translation in energy form takes place in the cells of the heart. The left ventricular myocytes are characteristically about 14 microns (μ) in diameter and 30–60 μ long, with many branching processes. Right ventricular cells are smaller and the atrial cells are smaller than right ventricular cells. The most striking feature of these cells is the array of cross-striations resulting from the arrangement of the myofilaments (Fig. 7). The basic unit of the contractile elements, the sacromere, consists of the structures between two Z bands as defined by polarization optics. In the stretched state, these are an I band adjacent to each Z band, followed by an A band and an H band. With full contraction of the sacrcomere the I band disappears. As seen in the electron microscope, these striations consist of alternating bands of filaments. One set, the actin or thin filaments, inserts into either side of a Z band and extends away from this structure in the long axis of the cell. The actin filaments interdigitate with a set of thicker filaments, the myosin filaments, to form a hexagonal array of six actin filaments around each myosin filament (Fig. 8). Thus, two sets of actin filaments are present in each sarcomere interdigitating with one set of myosin filaments. During contraction the actin filaments increase their overlap with the myosin until, under physiologic conditions, the Z band is adjacent to the myosin filaments with loss of the I band. During relaxation the Z band location is about 0.35 μ from the myosin filaments. Since this occurs at each end of the sarcomere the relaxed cardiac sarcomere measures about 2.2 μ and the contracted about 1.5 μ, a 30 percent change. The myosin filaments have lateral projections at which point two ATPases are located, and at these sites a bridge to the actin filament is formed during contraction. The forming and releasing of these bridges between actin and myosin is associated with shortening of the sarcomere. This reaction utilizes ATP generated by the extensive array of mitochondria present in the heart cells. The method by which ATP generated in the mitochondria is delivered to the myosin ATPase is not clear.

Striated muscle cells, including heart cells, have two systems of tubules (Fig. 9). The transverse or T system is

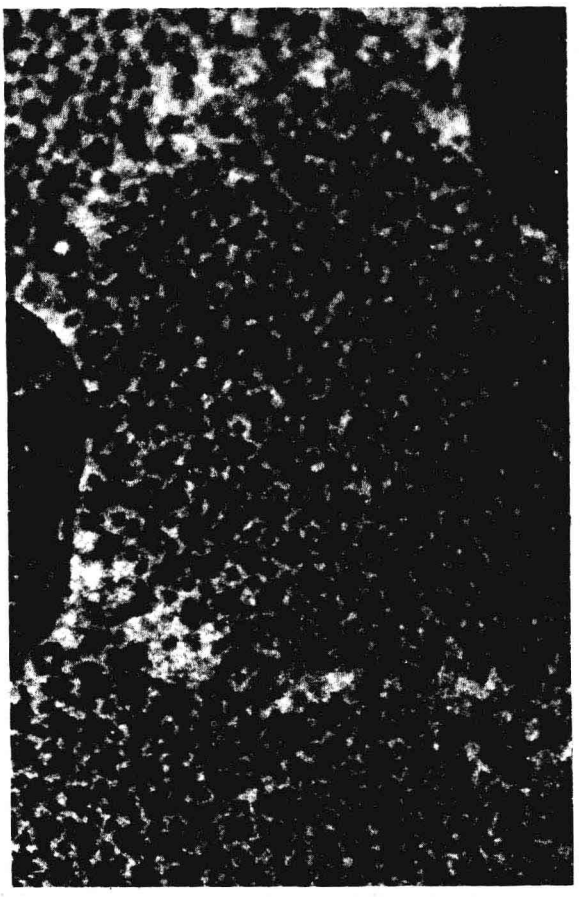

Fig. 8. Electron micrograph of guinea pig heart with cell cut in cross section. The circled area indicates the hexagonal array of actin filaments around a myosin filament. (× 160,000) (Courtesy of Miss A Ceselski, Department of Pathology, University of South Carolina, Columbia.)

an invagination of the surface membrane of the cell. This invagination occurs at a constant site for a given type of muscle. In heart muscle, this invagination occurs at the Z band as small tubules that surround each bundle of filaments. Since this system is an invagination, the lumen is in contact with the extracellular space, as can be experimentally demonstrated by the presence of intravascularly injected ferritin in this system deep within intact heart cells. Adjacent to small bulbous distensions of this T system and extending in the long axis of the cell between the bundles of filaments is the second tubular system, the longitudinal system. The transverse tubular system is an extension of the plasma membrane and conducts the depolarization wave deep within the cell, permitting almost simultaneous activation of all sarcomeres within the cell. The excitation wave entering via the transverse tubular system causes release of Ca^{++} from the longitudinal system. This is presumably initiated at the points of close contact between these two systems at the Z band in heart muscle. Ca^{++} release occurs from the longitudinal system and arrives in the region of the myosin ATPase. Activity of this Ca^{++}-modified ATPase, as well as a Mg^{++}-dependent ATPase, in the two heads on each light meromyosin molecule is associated with shortening of the sarcomeres and overall contraction of the heart.

Heart cells contain large numbers of mitochondria. These are located in the subsarcolemmal region, perinuclear region, and in rows between groups of myofilaments. The perinuclear region contains ribonucleoprotein particles, glycogen, and smooth-surfaced endoplasmic reticulum. The single nucleus is reasonably centrally located, unlike that of the skeletal muscle cell. Under conditions of marked hypertrophy, the nucleus enlarges and may actually divide in some fashion, resulting in a binucleate cell. Hypertrophy of the heart follows embryologic development, with accretion of sarcomeres at intercalated discs resulting in longer cells and in the subsarcolemmal region resulting in wider cells.

Contraction of isolated heart muscle is analogous to contraction of isolated skeletal muscle. There are differences, some of which have an anatomic explanation. One of the important differences is the ability of heart cells to propagate an impulse from one to another. This is accomplished at specialized regions of the sarcoplasmic membrane termed "tight junctions" or nexuses. These structures are present in a variety of cells where cell-to-cell impulse propagation is important, such as in smooth muscle cells and some nerve cells. These are points of low resistance, and depolarization at this point is transmitted to the adjacent cell that participates in the nexus. Disruption of these junctions results in marked increase in cell-to-cell resistance as measured by two electrodes within cells of the participating array. Also, with disruption of these junctions, stimulation of one cell does not result in propagation of the impulse, and thus the adjacent cells fail to contract.

These points of low resistance convert a multicellular organ, the heart, into an electrical syncytium, but the multicellular state of the heart permits activation of different units at different times. The subsequent contraction is progressive and coordinated in space and time. The presence of multiple small cells that transmit force in the cells' long axis requires that there be great adherence between cells in the line of force development. This is accomplished by intercalated discs, highly specialized regions of attachment found between heart cells that, in many respects, resemble desmosomes of epithelial cells.

The general description of heart cells holds for most atrial and ventricular cells with the exception that many muscle cells of the atria contain small granules. These granules are similar to storage granules seen in a variety of other cells. The content of these granules has not been completely defined.

There are highly specialized cells within the atria and ventricles that are quite different in form from that of the heart cells described. The most thoroughly studied are the Purkinje cells. These cells do not have a highly ordered array of myofilaments, and in some, only portions of unattached sarcomeres are present. The few poorly arranged