Cardiovascular Pathology

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Dedication

We dedicate this book to the memory of John J. Fenoglio, Jr., M.D.

John James Fenoglio, Jr., M.D., died on August 7, 1989, at the age of 46 after a long illness. At the time of his death, he was Professor and Vice Chairman of the Department of Pathology, Columbia University College of Physicians and Surgeons, Director of Medical and Pediatric Pathology, Director of the Division of Cardiovascular Pathology, and Attending Pathologist at Presbyterian Hospital in the City of New York.

Graduated from Harvard College and Georgetown University Medical School, Dr. Fenoglio came to the Columbia-Presbyterian Medical Center in 1968 for his residency in pathology under Dr. Donald W. King. He remained at this institution for all but three years of his professional career. Columbia-Presbyterian was truly his life's work. As a resident working in the laboratory of Dr. Bernard Wagner, Dr. Fenoglio soon became interested in cardiovascular pathology. This laboratory was applying histochemical and ultrastructural methods in the study of primary myocardial and valvular heart disease. Investigation of spontaneous cardiac disease in cats and dogs was carried out in conjunction with the Animal Medical Center in New York City. He was an early investigator of feline cardiomyopathy. John recognized that structure and function were inseparable and devoted much time to the clinical cardiologists, heart surgeons, and pharmacologists. There was further cardiovascular pathology training at the Armed Forces Institute of Pathology (AFIP), during which time he coauthored the fascicle devoted to tumors of the cardiovascular system.

Following his AFIP experience, John returned to the Columbia-Presbyterian Medical Center in 1977. He established the Division of Cardiovascular Pathology, and it was through his work in this division that new major scientific contributions were made. From his voluminous bibliography, some important themes stand out. Working in close collaboration with members of the Department of Pharmacology, John virtually pioneered the use of electron microscopy as an investigative tool, in conjunction with cardiac electrophysiology. John and Dr. Andrew Wit, for example, were particularly interested in the structural correlates of arrhythmias that may complicate myocardial infarction. During the early years of endomyocardial biopsy at the Columbia-Presbyterian Medical Center, John recognized the utility of this procedure in the diagnosis of inflammatory heart disease. Together with Dr. Melvin Weiss of the Department of Medicine, he developed a clinically useful diagnostic scheme for myocarditis, a forerunner of the Dallas criteria currently in use.

John's expertise in pathology and skill at directing discussions to useful ends made him a valuable advisor and ad hoc reviewer for the National Heart, Lung and Blood Institute. John was an excellent teacher whether his students were diagnostic pathologists, clinicians, residents, or sophomore medical students. His love of teaching was recognized by these second-year students who elected him "Teacher-of-the-Year" several times.

During recent years he was called upon to do more and more administrative work in *the Department of Pathology. First as Acting Chairman, then as Vice Chairman in charge of the diagnostic services, he provided direction and an unswerving course toward the pursuit of excellence. His straightforward approach, his ability to focus on the essence of a problem, and his firm guidance in resolving crises were much appreciated by all. Regrettably, Dr. Fenoglio's career was cut short, and many, many people will miss him.*

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Modern Pathology, January 1990

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The Role of Coronary Artery Lesions in Ischemic Heart Disease: Insights from Recent Clinicopathologic, Coronary Angiographic, and Experimental Studies

Preface

This book highlights specific areas of cardiovascular pathology that are of particular importance to a practicing pathologist. It provides an update on recent developments in the field of cardiovascular pathology by addressing current topics in which recent developments have changed accepted concepts. Chapter 1, The Examination of the Heart, will serve as a baseline for pathologists and as a guide for the optimal method of evaluating different heart diseases. New developments in diagnostic imaging techniques, recent concepts of pathophysiology, and advances in experimental studies require close interaction between the cardiologist and the pathologist to incorporate innovative ways to correlate the pathologic anatomy with the clinical findings.

The ever-increasing diagnostic modalities being introduced in medical science require a close working relationship between the clinician and the pathologist in order for progress to continue. Chapter 2, The Cardiologist as Clinician and Pathologist: The Interactions of Both and the Limitations of Each, examines specifically how this relationship can be optimized to yield maximum information.

Overall the book deals with four important areas of cardiovascular pathology: ischemic heart disease, cardiomyopathies, the use of endomyocardial biopsy in diagnosing heart and combined heart–lung transplant rejection and underlying heart disease, and valvular heart disease and pathology of native and prosthetic valves.

RENU VIRMANI, M.D.
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Chapter

1

EXAMINATION OF THE HEART

RENU VIRMANI, M.D., PHILIP C. URSELL, M.D.,
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The most common method of examination of the heart has been the opening of each of the four chambers according to the flow of blood.[1,2] Briefly, the right atrium is opened from the inferior vena cava to the tip of the atrial appendage; the right ventricle is opened along its attachment to the ventricular septum from the tricuspid annulus through the pulmonary outflow tract; the left atrium is opened by cutting across the roof of the atrium between the left and right pulmonary veins; and the left ventricle is opened laterally between the anterior and posterior papillary muscles to the apex and then cut along the anterior wall adjacent to the ventricular septum through the aortic outflow tract. The classic method produces an ideal teaching specimen; however, it is not optimal for evaluating certain types of pathologic processes in the heart. For example, the location and extent of a myocardial infarction may not be well demonstrated in a specimen opened in this manner. Newer clinical diagnostic imaging techniques and recent concepts of pathophysiology require diverse methods of dissection for effective correlation of cardiac anatomy.

TECHNIQUES FOR EXAMINATION OF THE HEART

Removal of the Heart

The examination of the adult heart begins after the anterior chest plate has been removed. A longitudinal cut through the anterior aspect of the pericardial sac is made. The amount of pericardial fluid is measured, and its character is noted. The surface of the visceral as well as parietal pericardium is also examined for exudates, adhesions, tumor nodules, or other lesions. A short longitudinal incision 2 cm above the pulmonary valve will enable a check for thromboemboli in the main pulmonary trunk *in situ*. The heart is removed by cutting the inferior vena cava just above the diaphragm and lifting the heart by the apex, reflecting

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it anteriorly and cephalad to facilitate exposure of the pulmonary veins at their pericardial reflection. After it is confirmed that the pulmonary veins enter normally into the left atrium, the pulmonary veins are cut. The aorta and the pulmonary trunk, the last remaining connections, are cut transversely 2 cm above the semilunar valves. Following removal of the heart from the pericardial cavity and before weighing the specimen, postmortem blood clots should be removed manually and gently by flushing the heart with water from the left and right atria.

Examination of Coronary Arteries

The ideal method of examining the coronary arterial tree requires injecting the coronary arteries with a barium-gelatin mixture and studying the vessels in radiographs.[3,4] Polyethylene tubing (Clay Adams, Intramedic, PE 190 to 240, usually PE 205), the tips of which may be flared in a flame, is used to cannulate each coronary ostium. The tubes are secured by a ligature at the origin of the coronary arteries, as close to the aorta as possible. The free end of each tube is attached to a hypodermic needle (usually size 16) on the barrel of a disposable syringe (usually 30 mL). The pressure of injection may be gradually increased to 100 to 120 mm Hg and maintained for 10 to 15 minutes. Following injection the cannulas are pulled out and the ligatures are tightened and knotted quickly. The heart is then fixed for 24 hours in formaldehyde with attention paid to maintaining normal three-dimensional relationships. After washing the fixed specimen in water, radiographs are made in anteroposterior as well as left and right anterior oblique positions (Fig. 1–1*A*). If the oblique positions are difficult to obtain, adequate information can be obtained with a superior view, that is, cephalad to caudal after the ventricles have been transversely sliced in a "bread loaf" manner (Fig. 1–1*B*).

The vessels that must be examined in all hearts include the four major epicardial coronary arteries: the left main, the left anterior descending, the left circumflex, and the right coronary arteries. However, when coronary angiography has been performed during life, attention must also be directed to smaller branches if the lumen of these vessels has severely reduced caliber. The smaller branches to be examined are the left diagonals, the left obtuse marginals, the intermediate and the posterior descending coronary arteries. Following postmortem radiography the coronary arteries are cut transversely at 3- to 5-mm intervals with a sharp scalpel blade by a gentle sawing motion (not by firm pressure) to confirm sites of narrowing and to evaluate the pathologic process (e.g., atherosclerotic plaques, thrombi, dissections) directly. If the coronary arteries are heavily calcified, it is desirable to remove the coronary arteries intact. Following dissection of the vessel from the epicardial surface, each coronary artery is carefully trimmed of excess fat and the intact arterial tree is placed in a container of formic acid for slow decalcification over 12 to 18 hours. Decalcification of isolated segments of vessel may be sufficient for cases in which the coronary arteries are only focally calcified.

The areas of maximal narrowing are noted by specifying the degrees of reduction of the cross-sectional area of the lumen (e.g., 0–25%, 26–50%, 51–75%, 76–90%, 91–99%, and 100%). Most cardiologists agree that, in the absence of other cardiac disease, significant coronary artery narrowing is that exceeding a 75% narrowing. Particular attention should be paid to the left main coronary artery, since disease in this vessel is very important clinically but frequently overlooked at autopsy.[5] Cross sections from areas of maximal narrowing from each of the four major epicardial coronary arteries are selected for histologic

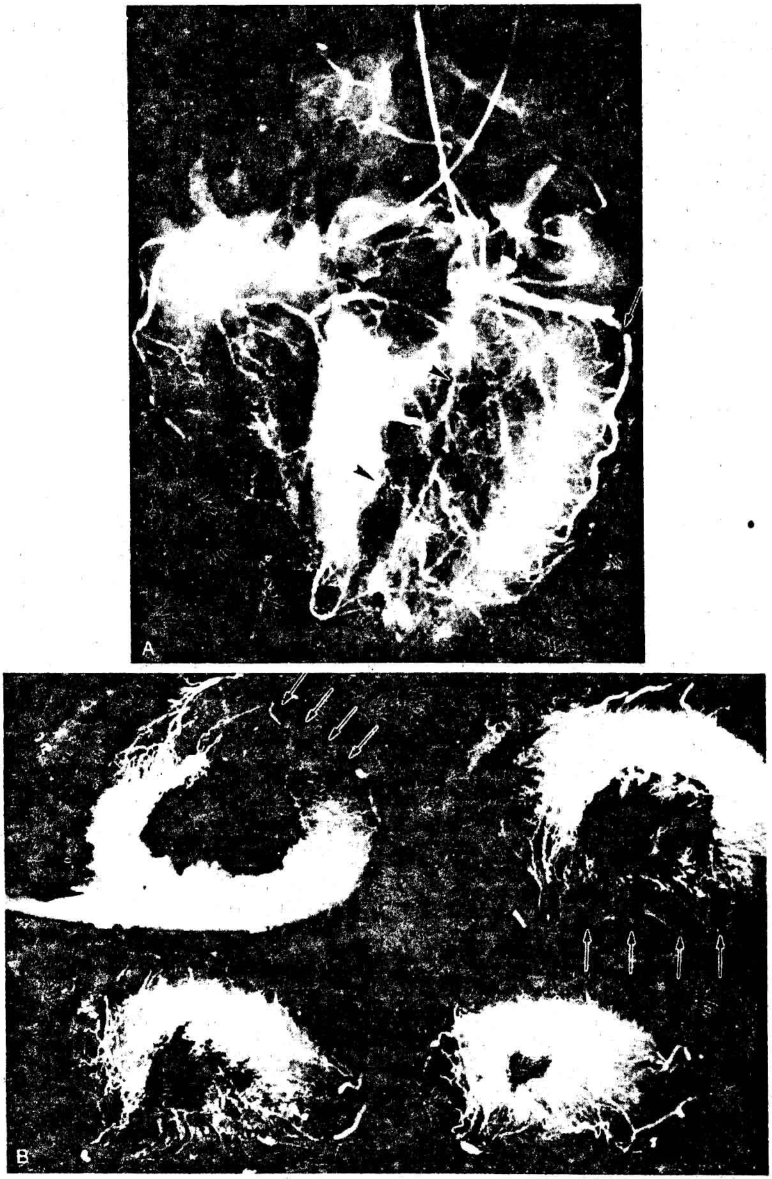

Figure 1–1. *A.* Radiograph of the heart in the anteroposterior plane after postmortem angiography demonstrates severe (>90% diameter reduction) narrowing of the proximal and distal portions of the left anterior descending coronary artery (*arrowheads*). The left circumflex artery shows diffuse irregularities with total obstruction of the takeoff of the left obtuse marginal artery (*arrow*). The right coronary artery also reveals severe disease in the distal portion. Note biventricular chamber dilatation in this 53-year-old man who died of ischemic cardiomyopathy. *B.* Radiograph of the ventricular slices after postmortem angiography in an 84-year-old man who jogged for 30 minutes, 3 days a week for the last 10 years of his life. The basal slice shows minimal filling of the arteries in the anterior wall (*arrows*), and histologically this correlated with transmural healed myocardial infarction (*upper left*). The second slide (*upper right*) from the base showed poor filling of the posterior wall of the left ventricle, and this correlated histologically with acute myocardial infarction. A thrombus was present in the right coronary artery.

examination. Sections of all coronary arteries containing thrombi are taken to aid in determining the time course of thrombogenesis.

Another method of fixation that is gaining popularity is perfusion fixation of the heart through the aorta at 100 mm Hg pressure with 10% buffered formaldehyde. A specially constructed Lucite plug is inserted into the aorta, taking care that the Lucite plug does not touch the aortic valve. The Lucite plug is attached to tubing that is connected to the perfusion chamber.[6] The latter is placed 130 cm above the specimen, and this provides gravity perfusion pressure that is equivalent to 100 mm Hg. As a result, the coronary arteries are fixed in a distended state that approximate the dimensions observed in living patients. Myocardial fixation is also affected, but cardiac chambers are not fixed in a distended state.

Examination of Bypass Grafts

When removing the heart at autopsy, care must be taken to avoid injury to the saphenous vein bypass grafts. A longer segment of the ascending aorta is left in continuity with the heart to enable examination of vein grafts from aortic orifice to distal anastomosis. Twists, as well as excessive tautness between aorta and distal anastomosis, are noted.[7] As in the native coronary arteries, the full extent of the saphenous vein grafts is best visualized radiographically. It is best to inject all the vein grafts simultaneously and to obtain radiographs before injection of the coronary arteries. This enables more detailed study of the native coronary arteries distal to the graft as well as at the coronary graft anastomosis. Measurements of lumen diameters may be made from the radiographs. In those cases in which the internal mammary artery is anastomosed to the left coronary system, the internal mammary artery is injected from where it has been severed during removal of the heart. The native coronary arteries are injected, fixed, and radiographed to evaluate the extent of disease in the remainder of the coronary arterial tree. The grafts and native arteries may then be removed from the heart, radiographed (Fig. 1–2), and cut at 3- to 5-mm intervals to determine the extent of luminal narrowing, the presence or absence of thrombi, and/or the extent of atherosclerosis in vein grafts and coronary arteries (Fig. 1–3).[8–11] In cases in which it is not possible to inject the vessels, the heart is fixed in 10% buffered formaldehyde overnight before dissection of the grafts and native vessels.

When there are no lesions identifiable grossly, random sections of the entire length of the grafts should be taken. Anastomotic sites are sectioned in different ways depending on whether the connection is end to end or end to side (see Fig 1–3).

Examination of the Myocardium in Ischemic Heart Disease

The myocardium is best examined for the presence or absence of acute or healed myocardial infarction by slicing the ventricles in a manner similar to a loaf of bread. To evaluate the specimen, a series of short-axis cuts are made through the ventricles from apex to base. This method is best accomplished using a long, sharp knife on the intact fixed specimen following examination of the coronary arteries. With the anterior aspect of the heart downward (against the cutting board), the cuts are made parallel to the posterior atrioventricular sulcus at 1- to 1.5-cm intervals from the apex of the heart to a point approximately 2 cm caudal to the sulcus. The result is a series of cross sections through the ventricles,

Figure 1–2. Radiograph of epicardial coronary arteries and saphenous vein bypass graft (*arrows*) to left circumflex (*LC*) removed at autopsy. Note calcification in native coronary arteries and absence of calcification in the vein graft. Also, a portion of the left anterior descending (*LAD*) coronary artery was surrounded by myocardium (bridging or tunneled coronary artery) (*TA*). (*R*, right coronary artery)

including papillary muscles with the atrioventricular valve apparatus left intact in the remainder of the specimen (Fig. 1–4). The location and extent of the infarct are noted. Locations may be stated using terms relating to the standard anatomic frame of reference (e.g., anteroseptal, posterolateral). The extent of infarction may be described in terms of circumference of the ventricle involved[12–14] and longitudinal portion of the ventricle involved (e.g., basal third, middle third, apical third) (Fig. 1–4*A* and *B*). The distribution within the wall is also described (e.g., transmural or subendocardial). The gross pathologic appearance of the myocardium serves as a relatively good index as to the age of the infarct but must be confirmed by histologic examination. Even if infarction cannot be identified grossly, it is important to section the myocardium in the distribution of diseased coronary arteries more extensively.

Examination of the Heart in Cardiomyopathy

The short-axis sectioning method described above serves well for the examination of the cardiomyopathic heart. Cardiac hypertrophy and dilation may be