TUMORS of the CARDIOVASCULAR SYSTEM

by

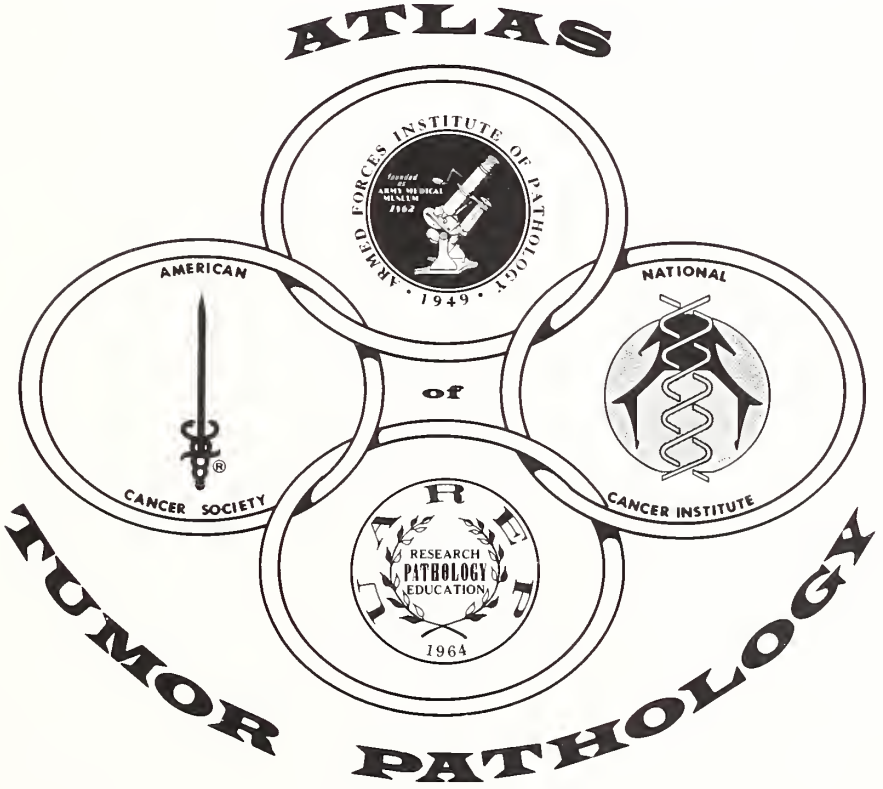
HUGH A. McALLISTER, JR., M.D.

and

JOHN J. FENOGLIO, JR., M.D.

AFIP

TUMORS
of the
CARDIOVASCULAR SYSTEM



ATLAS OF TUMOR PATHOLOGY

Second Series
Fascicle 15

TUMORS OF THE CARDIOVASCULAR SYSTEM

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ATLAS OF TUMOR PATHOLOGY

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EDITORS' NOTE

The Atlas of Tumor Pathology was originated by the Committee on Pathology of the National Academy of Sciences—National Research Council in 1947. The form of the Atlas became the brainchild of the Subcommittee on Oncology and was shepherded by a succession of editors. It was supported by a long list of agencies; many of the illustrations were made by the Medical Illustration Service of the Armed Forces Institute of Pathology; the type was set by the Government Printing Office; and the final printing was made by the press at the Armed Forces Institute of Pathology. The American Registry of Pathology purchased the fascicles from the Government Printing Office and sold them at cost, plus a small handling and shipping charge. Over a period of 20 years, 15,000 copies each of 40 fascicles were produced. They provided a system of nomenclature and set standards for histologic diagnosis which received worldwide acclaim. Private contributions by almost 600 pathologists helped to finance the compilation of an index by The Williams & Wilkins Company to complete the original Atlas.

Following the preparation of the final fascicle of the first Atlas, the National Academy of Sciences—National Research Council handed over the task of further pursuit of the project to Universities Associated for Research and Education in Pathology, Inc. Grant support for a second series was generously made available by both the National Cancer Institute and the American Cancer Society. The Armed Forces Institute of Pathology has expanded and improved its press facilities to provide for a more rapid and efficient production of the new series. A new Editor and Editorial Advisory Committee were appointed, and the solicitation and preparation of manuscripts continues.

This second series of the Atlas of Tumor Pathology is not intended as a second edition of the first Atlas and, in general, there will be variation in authorship. The basic purpose remains unchanged in providing an Atlas setting standards of diagnosis and terminology. Throughout the rest of this new series, the term chosen for the World Health Organization's series "International Histological Classification of Tumours" (when available) is shown by an asterisk if it corresponds to the authors' choice, or as the first synonym in bold print if it differs from the authors' heading. Hematoxylin and eosin stained sections still represent the keystone of histologic diagnosis; therefore, most of the photomicrographs will be of sections stained by this technic, and only sections prepared by other technics will be specifically designated in the legends. It is hoped that in many of the new series a broader perspective of tumors may be offered by the inclusion of special stains, histochemical illustrations, electron micrographs, data on biologic behavior, and other pertinent information when indicated for a better understanding of the disease.

The format of the new series is changed in order to allow better correlation of the illustrations with the text, and a more substantial cover is provided. An index will be included in each fascicle.

It is the hope of the Editors, past and present, the Editorial Advisory Committees, past and present, and the Sponsors that these changes will be welcomed by the readers. Constructive criticisms and suggestions will always be appreciated.

William H. Hartmann, M. D.
William R. Cowan, M. D.

William C. Manion, M. D. 1916–1970

The death of Dr. William C. Manion, in November 1970 at the age of 54 years, was a major loss to the staff of the Armed Forces Institute of Pathology and to his many friends and colleagues within the national and international medical communities. Dr. Manion had been deeply committed to patient care, and throughout his 18 years as Chief of the Cardiovascular Pathology Branch at the AFIP this commitment ordered his professional priorities.

During an era which produced a surge in the development of highly sophisticated diagnostic technics and cardiovascular surgery, Dr. Manion's consultative expertise was increasingly sought on thousands of surgical and autopsy cases. The vast amount of material which he assembled during his lifetime remains a valuable source of teaching and research potential. Among the several projects that intrigued Dr. Manion were plans for a series of monographs on tumors and cysts of the heart and pericardium that he believed would be a worthy contribution to the medical literature. Over the years, the repository of the AFIP was continually searched, and a large collection of cardiac tumors and cysts was assembled. His meticulous review of the world literature led to the establishment of an impressive reference file which he planned to incorporate into his monographs. At the time of his death, much of what he had accomplished had not been committed to paper; indeed, his death has deprived us of his written concepts of cardiac neoplasms. The archives of cases, however, remains a rich legacy that has grown with the addition of new entities during the intervening years, finally culminating in the publication of this Fascicle.

The full measure of Dr. Manion's death was felt as much in the loss of the man as of the pathologist. He was always available to colleagues and friends for counsel, guidance, or the exchange of ideas, and gave selflessly of his time and energies regardless of his own interests. His enthusiasm for medicine and pathology was infectious; he always expected the best from those around him, and gave, too, the best of himself. His accomplishments can be judged "not only by what he finished, but by what he set in motion." It is, therefore, to honor the human qualities of William Manion as much as his professional endeavors that we dedicate this Fascicle.

PREFACE AND ACKNOWLEDGMENTS

Since publication of the first fascicle on Tumors of the Cardiovascular System, numerous examples of primary tumors of the heart and great vessels have been carefully collected and catalogued in the Department of Cardiovascular Pathology of the Armed Forces Institute of Pathology, under the direction of the late Dr. William C. Manion and, subsequently, Dr. Hugh A. McAllister. This vast body of material has formed the basis for this volume which is not intended to replace the classic fascicle of Dr. Benjamin Landing and Dr. Sidney Farber, but rather to present new information on tumors of the heart and great vessels. The vasoformative lesions and tumors of the peripheral vascular system are not covered in this volume. These lesions are presented in detail in the original fascicle, Tumors of the Cardiovascular System, and under specific organ systems in the individual fascicles of the second series.

The number of primary tumors of the heart and pericardium available for review in the AFIP probably exceeds one half of all published cases in the world literature, and that portion of the current fascicle is based on these documented cases. Appropriate references, appearing at the conclusion of each section, primarily include major review articles but do not represent a total review of the literature on cardiac tumors. Our purpose is to present data from a large series of cases in which a definitive diagnosis has been established rather than to compile data from numerous published case reports in which diagnoses could not always be substantiated.

Unfortunately, the AFIP does not have a comparable volume of cases of tumors of the great vessels, and in this section we have had to rely on the literature. Since it is difficult in many instances to document the appropriate histologic diagnosis from the published descriptions, we have compiled the published experience on tumors of the great vessels and have not attempted to estimate the incidence of the various entities.

We wish to thank the many doctors who contributed interesting cases to the AFIP, and especially those who responded over the past two decades to Dr. Manion's personal requests for unusual cardiac tumors. Unfortunately, neither space nor circumstances permit individual acknowledgment of all contributors. Inevitable administrative changes over the years have depleted some of the files containing the names of many who undoubtedly deserve recognition. We are grateful to the following colleagues, whose correspondence remains, for their special interest in our quest for examples of cardiac neoplasms:

Dr. Giorgio Baroldi, Milan, Italy; Dr. Weldon K. Bullock, Los Angeles, California; Dr. J. N. P. Davies, Albany, New York; Dr. Israel Davidsohn, Chicago, Illinois; Dr. Mark Entman, Houston, Texas; Dr. Frank J. Glassy, Sacramento, California; Dr. Pedro Grases, Caracas, Venezuela; Dr. Antal Haraszti, Eger, Hungary; Dr. Gordon R. Hennigar, Charleston, South Carolina; Dr. Barton McSwain, Nashville, Tennessee; Dr. Erwin Uehlinger, Zurich, Switzerland; and Dr. Wallace N. Yater (deceased), Washington, D. C.

We are deeply indebted to the many individuals at the Institute who have toiled with us during the preparation of this fascicle. Most especially, we wish to thank Mrs. Marie Cunningham and Mrs. Grace Lawson who meticulously assisted in the time-consuming, often frustating compiling, indexing, and abstracting of volumes of reference material and cases; Mrs. Anna B. Kelly and Mr. Charles E. Edwards for their expertise and assistance in photography; Mr. John I. Dexter for his technical assistance in obtaining and preparing specimens selected for illustration; and Mr. Jerry L. Badders and staff for their critical advice and artistry in the design, layout, and printing of the color plates.

Judith Lawson, our most able secretary and editorial assistant, has endured with us throughout this project. More than anyone else, she deserves credit for the encouragement and support of our efforts to bring this material to publication as an ultimate realization of Dr. Manion's aspiration to give the medical community a definitive text on cardiovascular neoplasms.

Our appreciation is extended to Dr. Harlan I. Firminger and Dr. William H. Hartmann and the editorial staff for their unending patience. The constructive comments of Dr. Jack L. Titus and Dr. Gerald Fine were most helpful. Most especially, we wish to thank Mrs. Audrey Cyr who continually saw the light at the end of the tunnel.

Finally, we wish to extend a very special, warm tribute to Mrs. Billie Manion. Her quiet devotion to her husband in all his pursuits and her enthusiastic support of his professional endeavors were in a very real sense most important contributions to this work.

Hugh A. McAllister, M. D.
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TUMORS OF THE CARDIOVASCULAR SYSTEM

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TUMORS OF THE CARDIOVASCULAR SYSTEM

PRIMARY TUMORS AND CYSTS OF THE HEART AND PERICARDIUM

Primary tumors of the heart and pericardium are extremely rare, with an incidence between 0.0017 percent and 0.28 percent in reported or collected autopsy series. By 1968, approximately 700 primary tumors of the heart and pericardium, including cysts, had been reported. Since 1968, approximately 100 additional cases have been added to the literature. In total, between 800 and 1000 primary tumors and cysts of the heart and pericardium have been reported.

We have reviewed 533 primary tumors and cysts of the heart and pericardium from the files of the Armed Forces Institute of Pathology. This number includes only those cases for which adequate clinical histories and representative histologic slides or gross hearts were available. Having had the opportunity to review and assess the histologic findings of each case, we have elected not to include published statistics in our series, because the histology is frequently unclear and the reviewer must depend on the authors' diagnosis. This fascicle, therefore, is based on the AFIP collection, although pertinent information from other reports and appropriate references have been included.

The 533 primary cysts and tumors of the heart and pericardium in the AFIP collection are summarized in Table 1. A number of these lesions have previously appeared in the literature, either as single reports or in a collected series.

The most common cardiac tumor is the myxoma. Twenty-five percent of all tumors and cysts of the heart and pericardium are

TABLE 1

TUMORS AND CYSTS
OF THE HEART AND PERICARDIUM

Type	Number	Percent
Benign		
Myxoma	130	24.4
Lipoma	45	8.4
Papillary fibroelastoma	42	7.9
Rhabdomyoma	36	6.8
Fibroma	17	3.2
Hemangioma	15	2.8
Teratoma	14	2.6
Mesothelioma of the A-V node	12	2.3
Granular cell tumor	3	
Neurofibroma	3	
Lymphangioma	2	
Subtotal	319	59.8
Pericardial cyst	82	15.4
Bronchogenic cyst	7	1.3
Subtotal	89	16.7
Malignant		
Angiosarcoma	39	7.3
Rhabdomyosarcoma	26	4.9
Mesothelioma	19	3.6
Fibrosarcoma	14	2.6
Malignant lymphoma	7	1.3
Extraskeletal osteosarcoma	5	
Neurogenic sarcoma	4	
Malignant teratoma	4	
Thymoma	4	
Leiomyosarcoma	1	
Liposarcoma	1	
Synovial sarcoma	1	
Subtotal	125	23.5
Total	533	100.00

myxomas, and 40 percent of benign cardiac tumors are myxomas. In adults, almost half of the benign tumors are cardiac myxomas (Table 2). Approximately one-fourth of all tumors and cysts of the heart and pericardium are malignant. Of the malignant tumors, one-third are angiosarcomas; 20 percent are rhabdomyosarcomas, 15 percent are mesotheliomas, and 10 percent are fibrosarcomas.

In children and infants, the most common cardiac tumor is the rhabdomyoma (Tables 3 and 4). Malignant tumors are rare in the pediatric age group; they comprise less than 10 percent of all tumors

TABLE 2

TUMORS AND CYSTS OF THE HEART AND PERICARDIUM IN ADULTS*

Type	Number	Percent
Benign		
Myxoma	118	26.6
Lipoma	45	10.1
Papillary fibroelastoma	42	9.5
Hemangioma	11	2.5
Mesothelioma of the A-V node	9	2.0
Fibroma	5	1.1
Teratoma	3	
Granular cell tumor	3	
Neurofibroma	2	
Lymphangioma	2	
Rhabdomyoma	1	
Subtotal	241	54.3
Pericardial cyst	80	18.0
Bronchogenic cyst	6	1.4
Subtotal	86	19.4
Malignant		
Angiosarcoma	39	8.8
Rhabdomyosarcoma	24	5.4
Mesothelioma	19	4.3
Fibrosarcoma	13	2.9
Malignant lymphoma	7	1.6
Extraskeletal osteosarcoma	5	1.1
Thymoma	4	
Neurogenic sarcoma	3	
Leiomyosarcoma	1	
Liposarcoma	1	
Synovial sarcoma	1	
Subtotal	117	26.3
Total	444	100.00

*Patients 16 years of age and older.

TABLE 3

TUMORS AND CYSTS OF THE HEART AND PERICARDIUM IN CHILDREN*

Type	Number	Percent
Benign		
Rhabdomyoma	35	39.3
Fibroma	12	13.5
Myxoma	12	13.5
Teratoma	11	12.4
Hemangioma	4	4.5
Mesothelioma of the A-V node	3	3.4
Neurofibroma	1	1.1
Subtotal	78	87.6
Pericardial cyst	2	2.2
Bronchogenic cyst	1	1.1
Subtotal	3	3.4
Malignant		
Malignant teratoma	4	4.5
Rhabdomyosarcoma	2	2.2
Neurogenic sarcoma	1	1.1
Fibrosarcoma	1	1.1
Subtotal	8	9.0
Total	89	100.00

*Patients 15 years of age or younger.

and cysts of the heart and pericardium. In infants (less than one year of age), more than 75 percent of tumors and cysts are rhabdomyomas or teratomas. In children from one to 15 years of age, myxomas, rhabdomyomas, and fibromas are the most common cardiac tumors, in that order; these three tumors account for 80 percent of benign tumors and 60 percent of all tumors and cysts in this age group.

In this fascicle, tumors are classified on the basis of histologic type rather than by location. Generally, except for mesotheliomas of the atrioventricular (A-V) node and papillary fibroelastomas, and possibly myxomas, tumors of the heart and pericardium are similar histologically to tumors of the soft tissues.

TABLE 4

TUMORS AND CYSTS OF THE HEART AND PERICARDIUM IN INFANTS*

Type	Number	Percent
Benign		
Rhabdomyoma	28†	58.3
Teratoma	9	18.8
Fibroma	6	12.5
Hemangioma	1	2.1
Mesothelioma of the A-V node	1	2.1
Subtotal	45	93.7
Bronchogenic cyst	1	2.1
Subtotal	1	2.1
Malignant		
Fibrosarcoma	1	2.1
Rhabdomyosarcoma	1	2.1
Subtotal	2	4.2
Total	48	100.00

*Patients one year of age or younger.
†Includes 3 stillborn infants.

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BENIGN TUMORS AND CYSTS OF THE HEART AND PERICARDIUM

MYXOMA

SYNONYMS AND RELATED TERMS: Angioreticuloma; right atrial myxoma; left atrial myxoma; endothelioma; intracardiac endodermal heterotopia.

Definition. Myxoma is the most frequent primary tumor of the heart. It arises from the endocardium as a polypoid, often pedunculated tumor mass, extending into a cardiac chamber. Cardiac myxomas are derived from mesenchymal cells of the subendocardial layer and imitate primitive mesenchyme.

Clinical Aspects. The clinical presentation of the cardiac myxoma is most dependent upon the cardiac chamber involved by the tumor. The presentations of the 130 patients in the AFIP series are summarized in Table 5. For convenience, all patients with signs and symptoms of mitral valve disease are tabulated together.

Before 1960, cardiac myxomas were generally diagnosed as, and the patient treated for chronic rheumatic heart disease. Since that time, as new diagnostic methods of cardiology (cardiac catheterization and, most recently, echocardiography) have become available, and as clinicians have become increasingly aware of the ability of cardiac myxomas to imitate mitral valve disease, these tumors have been correctly diagnosed and surgically excised. Of the 57 patients with clinical signs and symptoms of mitral valve disease in this series, 56 had a myxoma in the left atrium; the other had a myxoma in the right atrium. Clinical symptoms included dyspnea, progressive or refractory congestive heart failure, systolic and diastolic murmurs, and atrial arrhythmias. There have been extensive reviews in the literature of the symptoms of patients with myxomas in the left atrium and the

TABLE 5

CARDIAC MYXOMA
CLINICAL PRESENTATIONS IN 130 PATIENTS*

Signs and symptoms of mitral valve disease	57
Embolic phenomena	36
No cardiac symptoms – incidental finding	16
Signs and symptoms of tricuspid valve disease	6
Sudden unexpected death	5
Pericarditis	4
Myocardial infarction	3
Signs and symptoms of pulmonary valve disease	2
Fever of undetermined origin	2

*One patient with multiple myxomas had signs and symptoms of mitral and tricuspid valve disease.

clinical basis by which these patients are distinguished from patients with intrinsic mitral valve disease. Although this distinction may be difficult by physical examination, murmurs of changing intensity and systemic findings, such as an elevated sedimentation rate or increased gamma globulin levels, may be of diagnostic aid. Myxoma should be suspected in any patient with signs and symptoms of mitral valve disease, especially of recent onset.

The second most common clinical presentation of patients with cardiac myxomas is embolic phenomena. In 36 patients in this series, the initial event was embolic and was present in patients with myxomas arising both in the left and right side of the heart. The six patients with pulmonary emboli from a right atrial myxoma created diagnostic problems. They each had persistent fever, changing murmurs, and progressive congestive heart failure—all are symptoms of recurrent pulmonary emboli. Of the patients with myxomas in the left atrium and ventricle, slightly more than one-third (12 patients) died of a cerebrovascular accident, and an embolic myxoma was found at necropsy. Symptoms in the remaining 18 patients were sudden hemiparesis, sudden diplopia, or sudden loss of blood supply in an extremity. The common denominator was sudden onset of symptoms of arterial occlusion, and, in retrospect, these patients had either cardiac murmurs, often of changing intensity, or atrial arrhythmias. Many of these tumors were diagnosed following an arterial embolectomy. Occasionally, the myxoma was not recognized microscopically, and some patients had repeated episodes of peripheral embolization before a cardiac myxoma was suspected. All but one of the patients with a myxoma in the left ventricle presented with signs and symptoms of embolic phenomena. The association of arterial occlusion of sudden onset with cardiac murmurs, especially of varying intensity, should alert the clinician to the possibility of a cardiac myxoma.

An additional 18 patients had episodes of arterial embolic occlusion during the course of their disease or evidence of myxoma emboli at autopsy. Three patients who presented with signs and symptoms of myocardial infarction had a myxoma embolus in at least one coronary artery at necropsy.

Patients with a myxoma in the left side of the heart most frequently have symptoms of mitral valve disease or of embolic phenomena. These were the presenting symptoms in 86 of 108 patients with myxomas of the left atrium or ventricle in our series. In the remaining patients, multiple cardiac myxomas were present or the myxoma was an incidental finding at the time of necropsy.

In contrast to myxomas in the left side of the heart, those arising in the right side of the heart may mimic any number of clinical entities. In addition to pulmonary embolic phenomena, patients with myxomas in the right atrium or ventricle may have signs and symptoms of tricuspid valve disease (frequently diagnosed as Ebstein's deformity), of pulmonary stenosis, or of pericarditis and may even present with fever of undetermined origin. A myxoma should be suspected when signs and symptoms of tricuspid or pulmonary valvular disease develop, especially when the cardiac murmurs are variable, as they so frequently are in patients with myxomas in any cardiac chamber. Rhythm disturbances, especially right bundle branch block and atrial flutter or fibrillation, and ab-

normal peaked P waves on electrocardiogram are frequently seen in patients with a myxoma in the right side of the heart. They should alert the clinician to the possibility of a cardiac myxoma, especially in a patient with signs and symptoms of pericarditis or with a fever of undetermined origin. As with myxomas on the left side of the heart, newer advances in diagnostic cardiology have greatly aided in the diagnosis of right atrial and right ventricular myxomas.

Nine percent of the patients in our study were in the pediatric age group (15 years or under). The youngest patient was four years old. We have never seen a myxoma in a newborn or young infant. More than 50 percent of the patients with cardiac myxoma were in their fourth, fifth, and sixth decades; however, myxomas occur in all age brackets, and 12 percent of our patients were over age 70. Most series indicate a nearly equal sex distribution.

Description. Although cardiac myxomas differ in clinical presentation, depending on the chamber in which they are located, they are similar in gross and microscopic appearance, irrespective of their location. Sites of myxomas in the AFIP series are summarized in Table 6. The myxomas were multiple in 5 percent of the patients. In all these patients, one tumor arose in the left atrium, and symptoms were most frequently due to this myxoma. In three patients, however, a second myxoma was situated on the right side of the heart, and in one patient, a myxoma was present in each of the four cardiac chambers. Most myxomas arising in the atria, either left or right, are attached to the atrial septum, usually in the region of the limbus of the fossa ovalis. Only 1 of the 10 ventricular myxomas was attached to the ventricular septum. Atrial myxomas do not invariably originate from the atrial septum; 10 percent of the atrial myxomas in our series originated from sites in the atria other than the septum. After the atrial septum, the most common site was the posterior atrial wall, followed by the anterior atrial wall and the atrial appendage. We have never seen a myxoma arising from a cardiac valve.

Grossly, myxomas are usually polypoid, friable, and pedunculated, although some may be smooth-surfaced and rounded. Many myxomas have a short, broad-based attachment. True sessile myxomas are a rarity, if they exist at all. The majority of so-called sessile myxomas have previously embolized, leaving only the broad base of the polypoid tumor attached to the endocardium. Myxomas are soft and gelatinous, almost mucoid in appearance, and gray to gray-white, often with areas of hemorrhage or thrombus. Their size varies from 1 cm. up to 15 cm. in diameter, although the majority of myxomas are 5 to 6 cm. in diameter (figs. 1—7).

TABLE 6

CARDIAC MYXOMA
LOCATION OF
138 MYXOMAS IN 130 PATIENTS*

Site	Number	Percent
Left atrium	103	74.5
Right atrium	25	18.1
Right ventricle	5	3.7
Left ventricle	5	3.7

*Multiple myxomas were present in 6 patients.

Figure 1
MYXOMA
(Figures 1 and 2 from same case)

A cardiac myxoma fills the left atrium. The majority of myxomas consist of multiple, friable, polypoid fronds and have a distinctive mucoid or gelatinous appearance. Approximately 75 percent of cardiac myxomas arise in the left atrium, as illustrated here, and 18 percent arise in the right atrium.

Figure 2
MYXOMA

The most common site of attachment of myxomas in the left atrium (fig. 1) is the atrial septum adjacent to the fossa ovalis. The fronds of the myxomas are extremely friable and embolization is a common occurrence. Extreme care must be taken during surgical removal of the myxoma to avoid operative embolization.

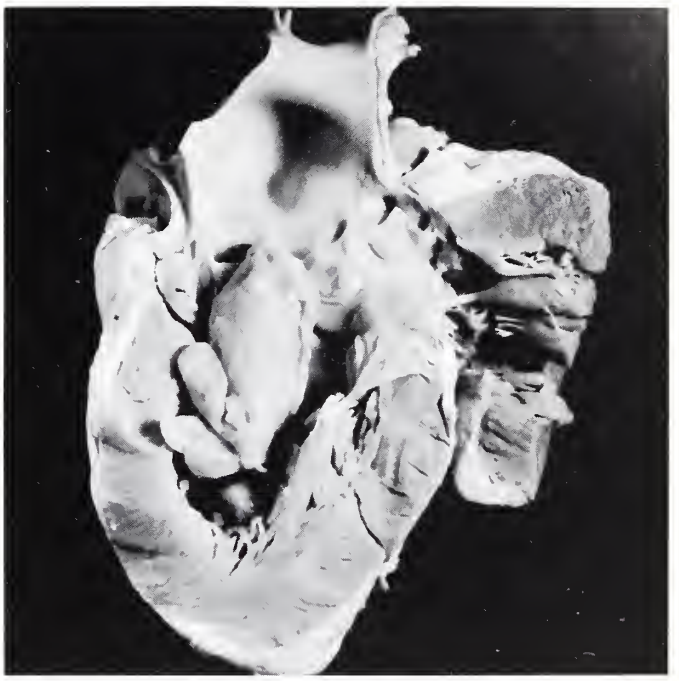

Figure 4
MYXOMA

Approximately 7 percent of myxomas arise in the ventricular cavities, nearly equally divided between the right and left ventricles. In the left ventricle, as shown here, the myxomas are molded in appearance and frequently obstruct the aortic valve. In 5 percent of patients, myxomas are present in more than one cardiac chamber.

Figure 3
MYXOMA

Myxomas often reach such proportions that they fill the atria and project through the valve into the ventricular cavity. This may produce valvular insufficiency and is responsible for the moving shadow across the valve seen by angiography.

Figure 5
MYXOMA

Although the majority of myxomas are polypoid and friable, a significant percentage are rounded and solid. Although the surface is smooth, it is glistening and gelatinous and foci of hemorrhage and thrombus are frequently present. In the left atrium, shown here, rounded myxomas arise most frequently from the atrial septum. A distinct groove is present around the myxoma near the distal end. This groove is caused by the myxoma protruding into, and obstructing the mitral orifice during diastole.

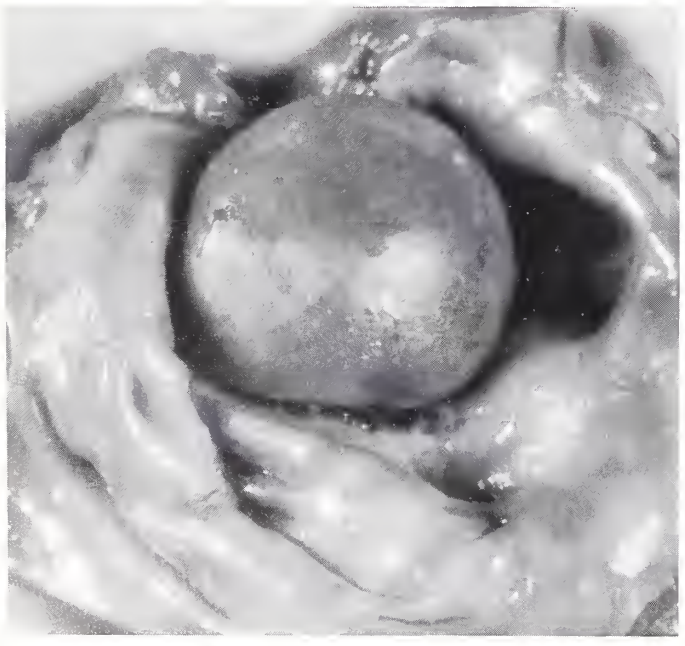

Figure 6
THROMBUS IN LEFT ATRIUM

Ball thrombi resembling rounded myxomas can also be found in the left atrium; however, thrombi are most commonly seen in patients with mitral valvular disease. Unlike the myxomas, ball thrombi are perfectly rounded with a smooth, polished appearing surface. The thrombi are firm and only loosely attached to the endocardial surface.

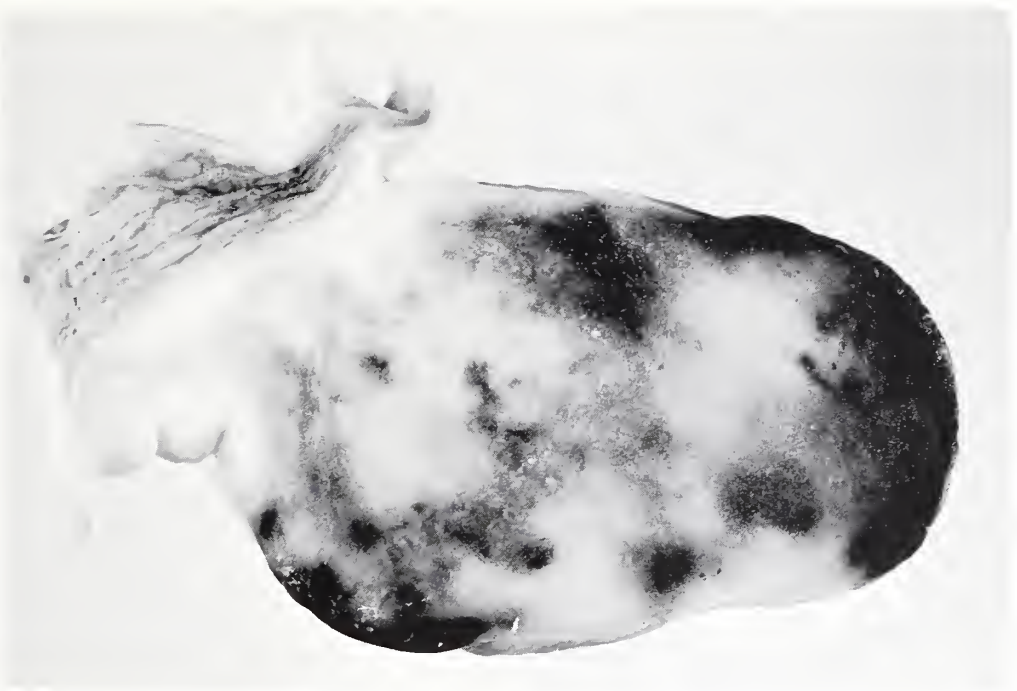

Figure 7
MYXOMA
(Figures 7 and 8 from same case)

On cross section, the broad base of attachment of the myxoma to the atrial septum is quickly appreciated. Foci of hemorrhage which appear black are present throughout the myxoma, and occasionally extend to the surface. These hemorrhages are, in part, artifacts of the operative removal of the myxoma. The thin-walled vascular channels in the myxoid stroma are easily disrupted.

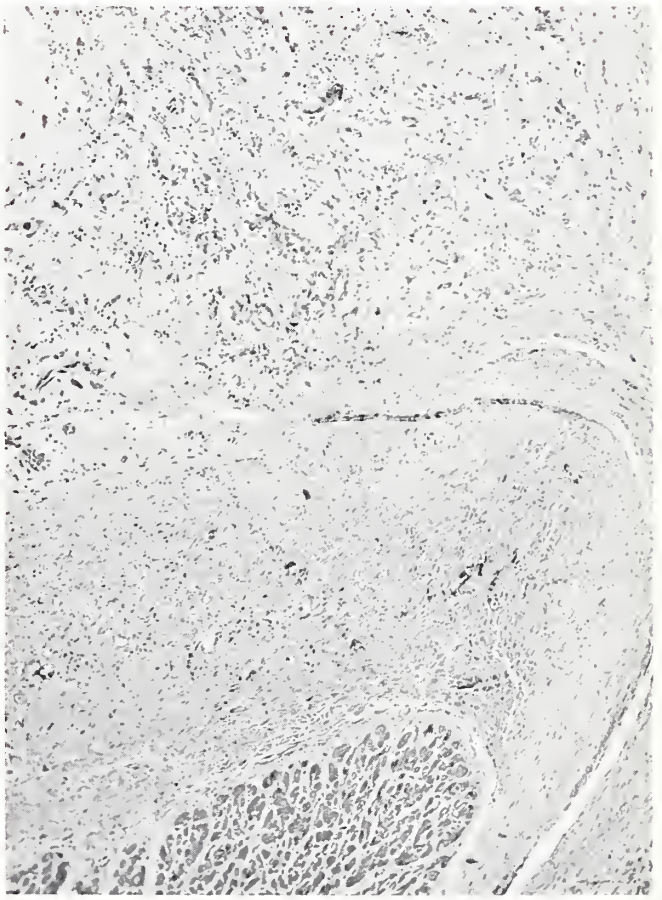

Figure 8
MYXOMA

Microscopically, the base of the myxoma in figure 7 extends into the underlying region of the heart. In the atrial septum, as illustrated, myxomas extend into the subendocardium, and atrial myofibers may be frequently trapped in the myxoma. Wide local excision is needed to assure that the myxoma does not recur. Complete excision of the atrial septum at the site of attachment in either the right or left atria has been advocated. Hematoxylin and eosin stain.* X55.

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*Throughout the fascicle where the stain is not so designated, hematoxylin and eosin stain has been used.

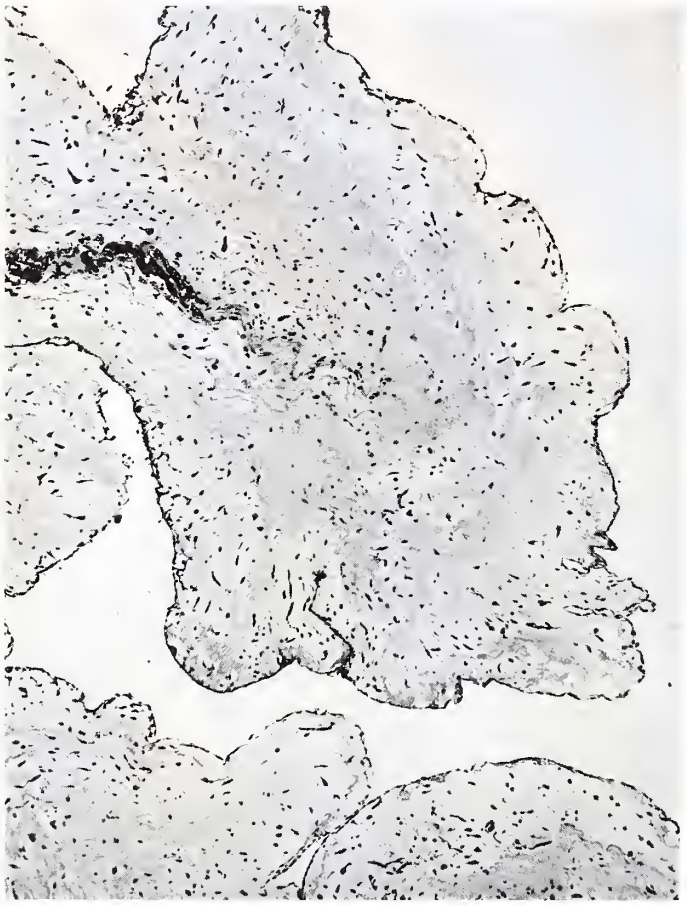

Figure 9
MYXOMA
(Figures 9 and 10 from same case)

The myxoma consists of an acid mucopolysaccharide matrix within which are embedded polygonal cells and occasional blood vessels. The surface of the fronds of the myxoma are covered by cells similar to those embedded in the matrix. X35.

Figure 10
MYXOMA

The myxoma (figure 9) matrix is often pale staining and granular, and the polygonal cells are embedded in the matrix singly or in small clusters. X100.

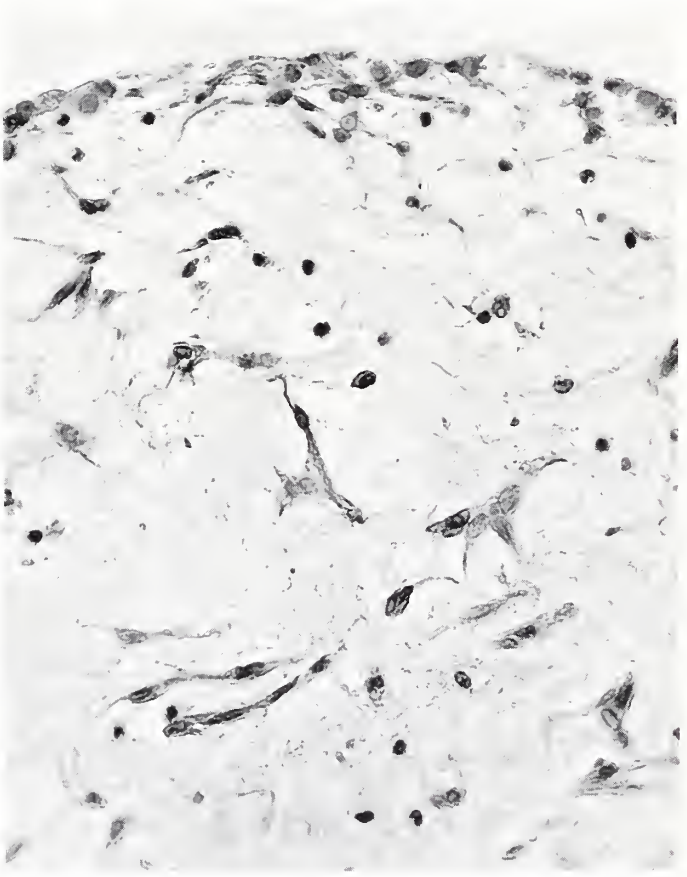

Figure 12
MYXOMA

The polygonal cells within a myxoma are often stellate as are those in the center of this photomicrograph. These cells may assume almost any configuration, however, and may be small and rounded, or elongated. The elongated cells are often arranged end to end in long cords of cells. X305.

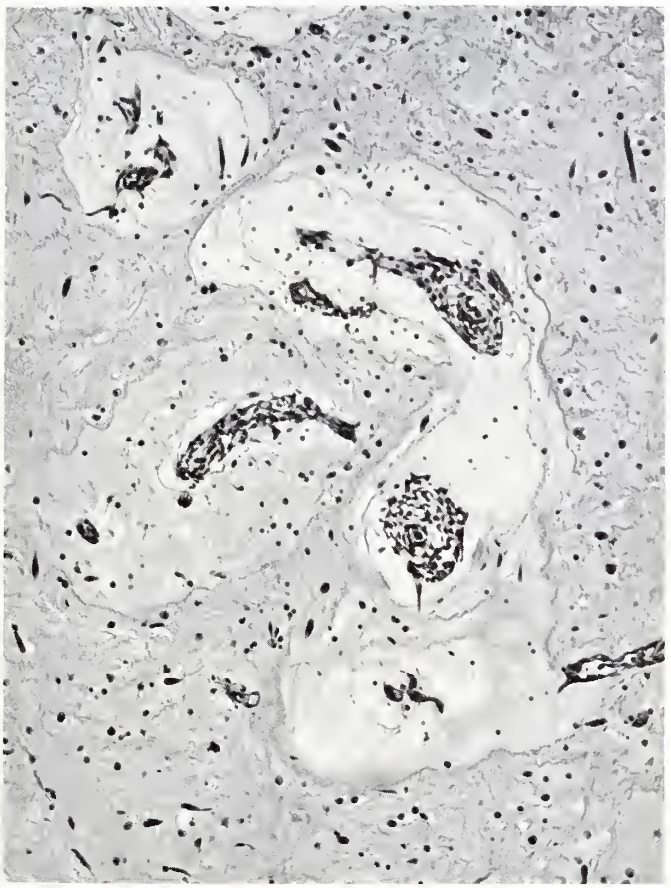

Figure 11
MYXOMA

In other areas within a myxoma, the matrix is more deeply staining and reticulin fibers and occasional strands of collagen are evident in the matrix. Polygonal cells are scattered throughout this denser matrix; however, many more polygonal cells are clustered in islands of loose matrix, often around small vascular channels. X90.

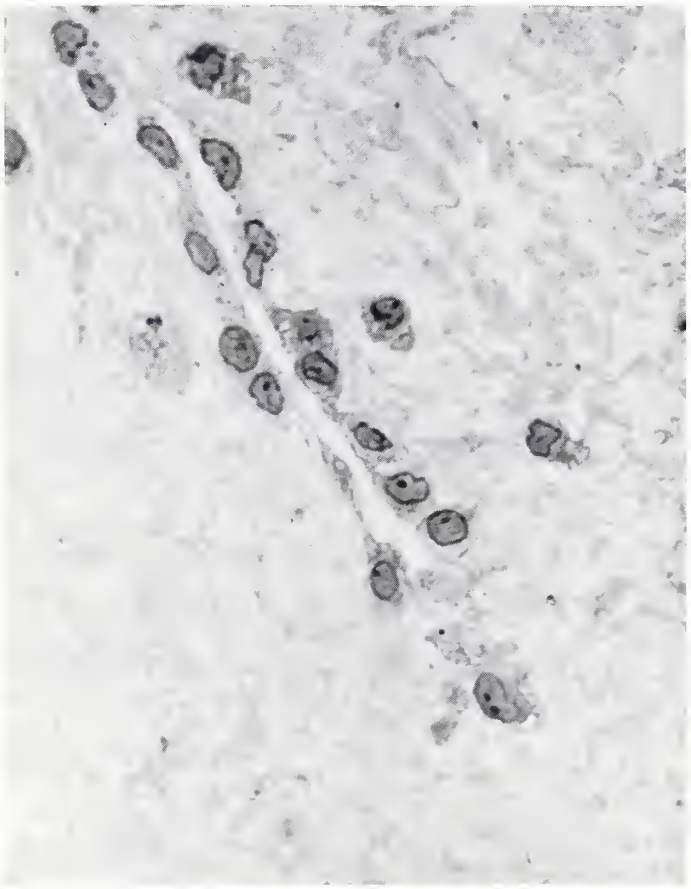

Figure 13
MYXOMA
(Figures 13, 17, and 19 from same case)

Frequently, the elongated cells within a myxoma form true channels lined by the elongated cells. These channels occasionally communicate with the surface of the myxoma. More often, these channels are filled with red blood cells and are embedded deep within the myxoma. The cells lining these channels resemble endothelial cells. Ultrastructurally, they more closely resemble multipotential mesenchymal cells. Intermediate forms between multipotential mesenchymal cells and primitive endothelial cells are frequent. This has suggested to many authors that the myxoma is derived from multipotential mesenchymal cells. Toluidine blue stain, X600.

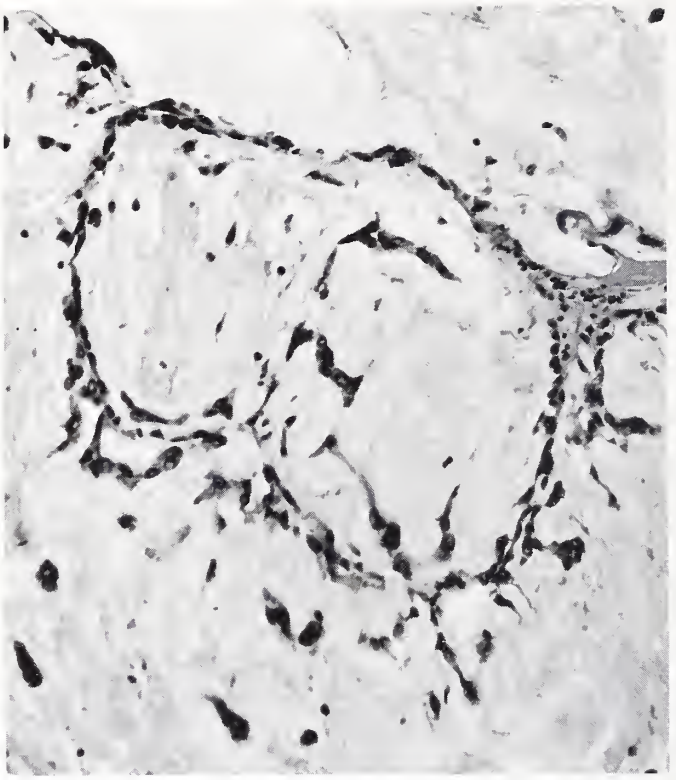

Figure 14
MYXOMA

The surface of a myxoma is covered by cells which resemble the endocardial cells that line the chambers of the heart. The surface cells are usually arranged in a monolayer; however, foci of multilayered, hyperplastic cells, as shown here, are frequent. In these areas, the hyperplastic surface cells extend in crypts into the myxoma and appear to merge with the multipotential mesenchymal cells of the matrix, suggesting that the surface cells are also derived from the multipotential mesenchymal cells. X150.

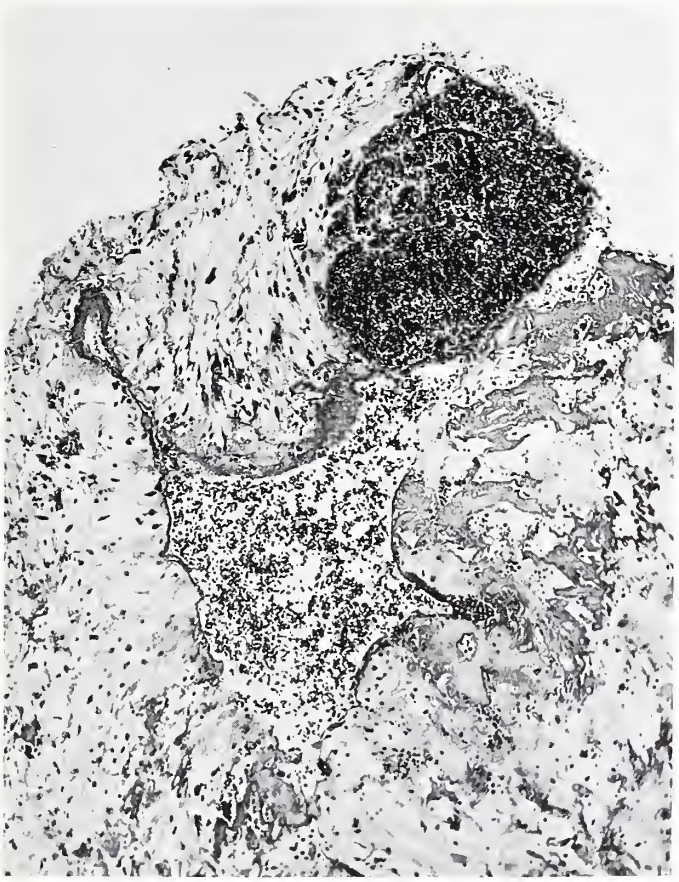

Figure 15
MYXOMA

The surface of a myxoma is focally covered by deposits of fibrin and erythrocytes, as in this illustration, and, occasionally, by organized thrombus. The accumulations of fibrin and the focal areas of hemorrhage are often in surface depressions devoid of surface cells, suggesting that the fibrin deposition and focal thrombus formation are secondary to trauma (evulsion of a portion of the myxoma). X50.

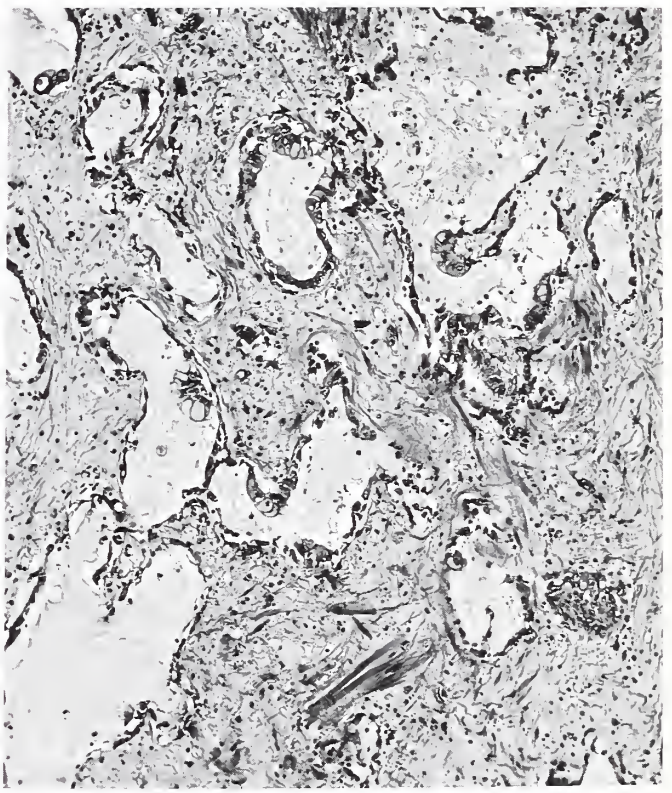

Figure 16
MYXOMA

Glandular-like spaces may be encountered in a myxoma, especially at the base of the tumor. The gland-like space or cysts are lined by the same polygonal cells or lepidic cells encountered in the matrix of the myxomas, and often are filled with amorphous material. This material consists of acid and neutral mucopolysaccharides and stains positively with acid mucopolysaccharide stains and, occasionally, with the periodic-acid Schiff reaction (PAS). X80.

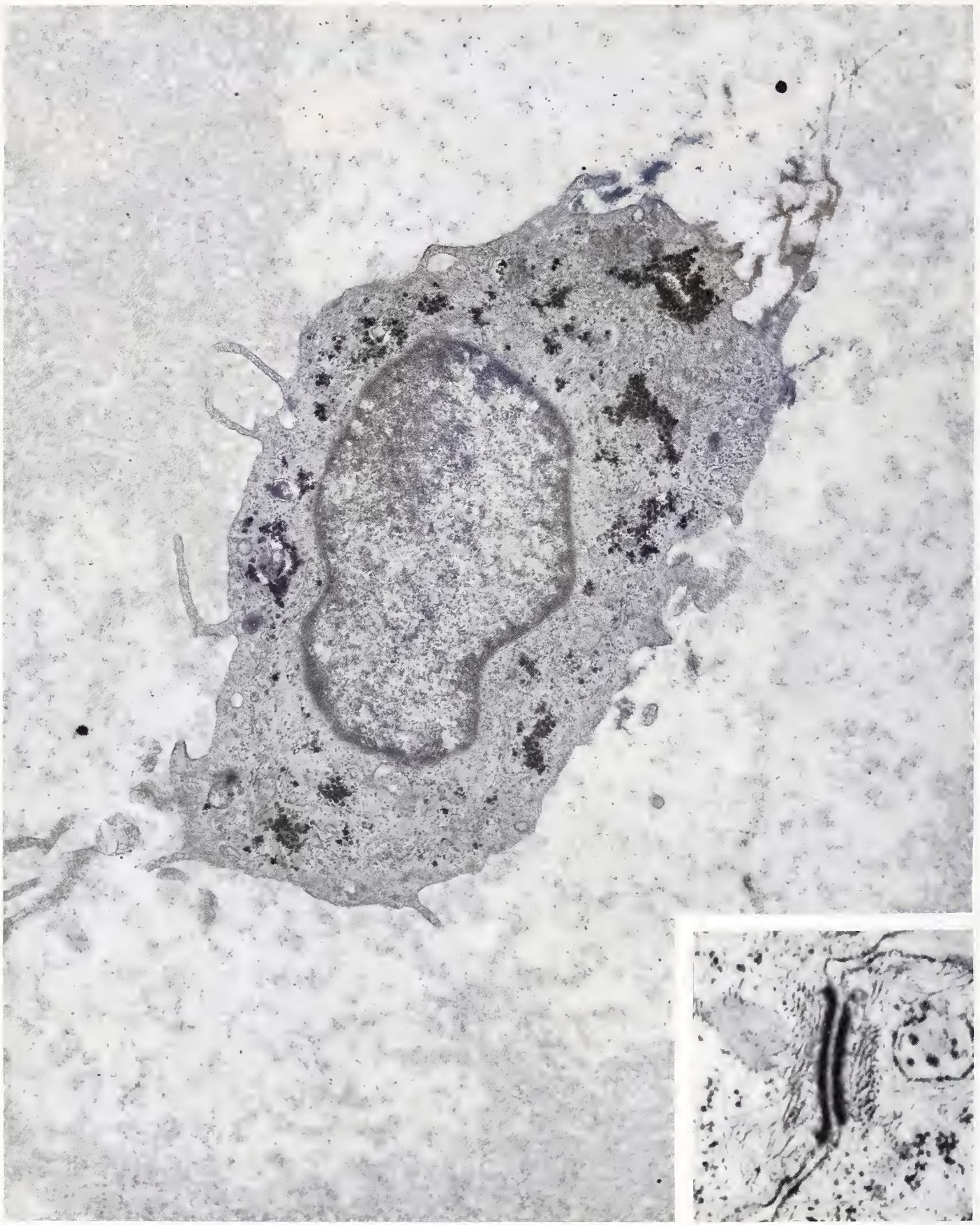

Figure 17
MYXOMA

Ultrastructure of a single myxoma cell (same tumor as figure 13) set in the granular appearing acid mucopolysaccharide matrix. The nucleus is large and surrounded by a prominent fibrous lamina. Within the cytoplasm are numerous electron-dense granules, many of which are within lysosomes. Occasionally, the myxoma cells are joined by specialized junctions of the desmosome type (insert). Ultrastructurally, myxoma cells resemble the multipotential mesenchymal cells of the subendocardial regions of the heart and the primitive mesenchymal cells described in the yolk sac. Uranyl acetate and lead citrate, X7700; Insert: X32,500.

Microscopically (figs. 8–16), myxomas consist of a myxoid matrix composed of acid mucopolysaccharide within which are embedded polygonal cells ("lepidic cells"), with scant eosinophilic cytoplasm. These cells are arranged singly, often assuming a stellate shape, and in small nests; they are occasionally multinuclear. The surface of the myxoma is covered by these polygonal cells, usually in a monolayer, but with focal clustering. These cells also form vascular-like channels (fig. 13) which represent both invaginations of the surface cells and replication of primitive capillaries. Ultrastructurally, the polygonal cells closely resemble multipotential mesenchymal cells (fig. 17). Throughout the myxoid stroma, there are variable amounts of reticular fibers, collagen, elastic fibers, and smooth muscle cells. Large blood vessels (arteries and veins) are abundant at the base of the tumor and are derived from the subendocardium. Lymphocytes and plasma cells are not infrequent, especially at the site of attachment in the subendocardium, and foci of extramedullary hematopoiesis are occasionally found (fig. 18). Foci of microscopic calcification were present in 10 percent of the myxomas in this series, and areas of bone formation, complete with hematopoietic tissue, occasionally occur.

Arguments supporting a thrombotic origin of cardiac myxomas that have recently appeared in the literature are without foundation. Proponents of this view have failed to consider, or have ignored, the following points: (1) Mural thrombi, even in the atria, organize into fibrous tissue; myxomas never do; (2) fluid influx into the lesion in the low pressure system of the atria cannot explain the myxomatous appearance of myxomas arising in the ventricles; and (3) mural thrombi are most frequent in patients with underlying cardiac disease and occur most often in the right atrium and right atrial appendage. Underlying cardiac disease is infrequent in patients with myxomas and most myxomas arise in the left atrium, usually from the atrial septum. Myxomas arising from the atrial appendage of either atrium are a distinct rarity (one case in this series). The most compelling argument against the thrombotic origin of the cardiac myxoma is based on tissue culture work (fig. 19). When thrombi are placed in tissue culture, fibroblasts overgrow the tissue culture, as is true of cultured granulation tissue. The cells obtained from cultured cardiac myxomas are mononuclear or multinuclear, and

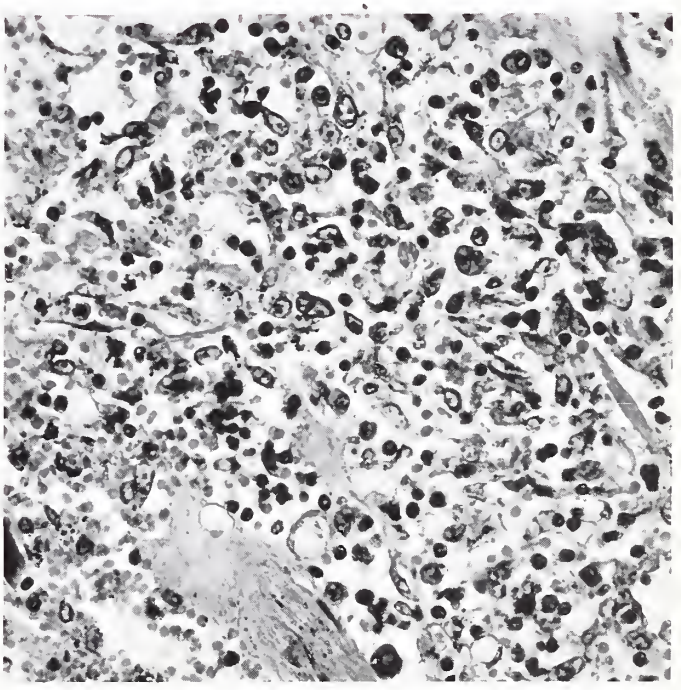

Figure 18
MYXOMA

Foci of extramedullary hematopoiesis, as shown here, as well as collections of plasma cells, and groups of large histiocytes are common in myxomas, especially at the base of the tumor. X300.

polygonal. These tissue-cultured cells closely resemble the multipotential mesenchymal cells which are ultrastructurally characteristic of the cardiac myxoma.

Embryonal rests have been reported in the heart in the region of the limbus of the fossa ovalis, and many authors have speculated that cardiac myxomas arise from these tissue rests. Although embryonal rests may occur in this region, more frequently clusters of "cardiac reserve" cells (multipotential mesenchymal cells) are found.

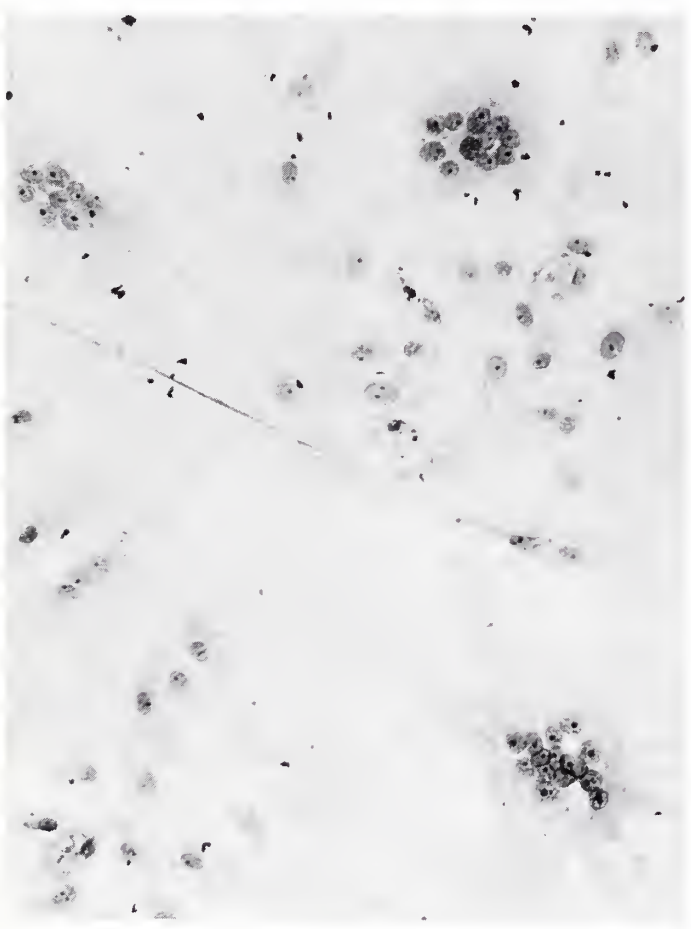

Figure 19
MYXOMA
When grown in tissue culture, myxoma cells (same tumor as figure 13) tend to aggregate into large multinuclear cells. The cells in the monolayer are polygonal with abundant cell contact with adjacent cells. A matrix material which stains positively for acid mucopolysaccharide is occasionally found, but collagen formation is not seen. Toluidine blue stain, X350.

Multipotential mesenchymal cells are a feature of loose connective tissue throughout the body. In the heart, loose connective tissue is found predominantly in the subendocardial region, especially in the atria and atrial septum, and in the cardiac valves. (Loose connective tissue of the cardiac valves differs from loose connective tissue elsewhere in the heart in that it is avascular and relatively acellular.) The multipotential mesenchymal cells are able to differentiate into fibroblasts, smooth muscle cells, and endothelial cells, and probably elaborate in part the acid mucopolysaccharide matrix of loose connective tissue (fig. 20). These components are also found in the cardiac myxoma. We propose that the cardiac myxoma is derived from multipotential mesenchymal cells of the subendocardium.

True myxomas do not occur on the cardiac valves, perhaps because of the relative lack of mesenchymal cells in the loose connective tissue component of the valves. The papillary tumors of cardiac valves differ from myxomas (see papillary fibroelastoma), and replicate the components of the endocardium rather than the subendocardium.

The evidence is overwhelming that the cardiac myxoma is a true neoplasm. (1) The cardiac myxoma is an expansive growth derived from a single cell type—the primitive or multipotential mesenchymal cell; (2) the cardiac myxoma is similar in appearance to true myxomas occurring elsewhere in the body (see "Tumors of the Soft Tissues", Fascicle 1, Second Series); and (3) if not completely excised, the cardiac myxoma can recur. Although the cardiac myxoma may recur, we have never seen an example of malignant cardiac myxoma. In the reported cases we have had

the opportunity to review, the malignant cardiac myxomas were examples of other malignant tumors (i.e., liposarcoma or rhabdomyosarcoma) with extensive areas of myxoid degeneration, or multiple benign myxomas. Such tumors were termed "myxoid imitators" by Stout and Lattes in "Tumors of the Soft Tissues", Fascicle 1, Second Series. Those authors have never seen a malignant example of a soft tissue myxoma.

Treatment. Complete surgical excision of the myxoma and its base is the treatment of choice. Surgical excision should not be unduly delayed because of the high incidence of embolization (fig. 21). As is now well recognized, special care must be taken during operation to avoid embolization, and all cardiac chambers should be explored for the occasional multicentric tumor. Long term follow-up was available to us in 33 patients who had surgical ex-

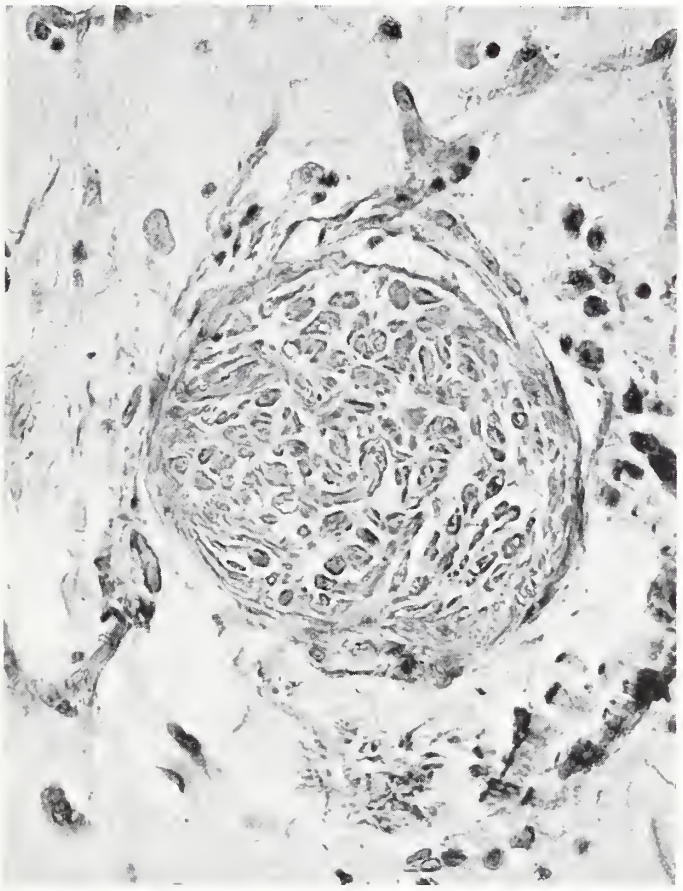

Figure 20
MYXOMA

Smooth muscle cells interspersed throughout the matrix are often numerous in myxomas. Occasionally, collections of larger, apparently branching cells, as illustrated, are suggestive of striated muscle in general and cardiac muscle in particular. Cross-striations, however, are not identifiable. The finding of striated muscle would be consistent with the proposed primitive mesenchymal origin of the myxoma, and especially appropriate if the myxoma arises from yolk-sac remnants often found in the heart, particularly around the fossa ovalis. X275.

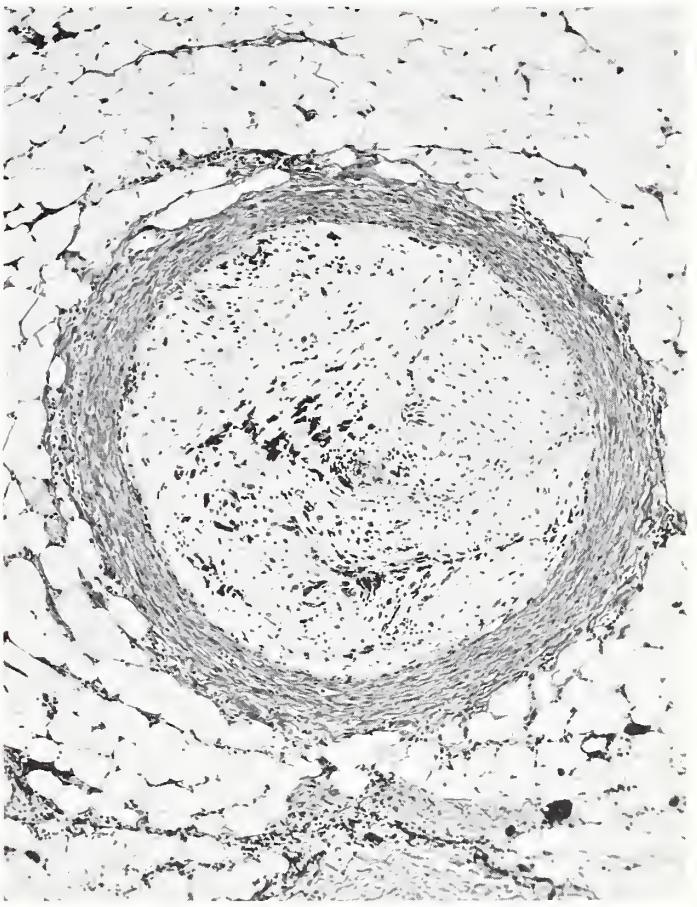

Figure 21
MYXOMA

Emboli from cardiac myxomas are a frequent occurrence. Myxoma emboli differ from thrombi. They are gelatinous, soft, and white-gray. Microscopically, they contain large polygonal cells embedded in an acid mucopolysaccharide matrix. Retrograde thrombus formation almost always occurs, making it imperative that the entire embolus be sectioned to find the underlying myxoma embolus. In this patient, the myxoma embolized to a coronary artery and the patient died of an acute myocardial infarct. X50.

cision of a cardiac myxoma. Of these patients, two were dead four and six years postoperatively of causes unrelated to their heart. In both patients, no residual myxoma was found at autopsy. A third patient died two years following excision of a cardiac myxoma of a myocardial infarct; an autopsy was not performed. The surviving 29 patients were alive and well at least two years following operation, and nine patients have been followed for more than 10 years without evidence of recurrence or metastasis.

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PAPILLARY FIBROELASTOMA

SYNONYMS AND RELATED TERMS: Myxoma of cardiac valves; papillary tumor of cardiac valves; fibromyxoma; hyalofibroma; hemangiofibroma; giant Lambl's excrescences; papilloma of valve.

Definition. These tumors are derived from the endocardium and, as such, consist of the normal components of the endocardium, fibrous tissue, elastic fibers, and smooth muscle cells set in a mucopolysaccharide matrix and covered by hyperplastic endocardial cells. Like the endocardium proper and the cardiac valves, these structures are avascular. We prefer the designation "papillary fibroelastoma," since this term describes both the gross and microscopic appearance of this tumor.

Clinical Aspects. In the vast majority of patients, these tumors are incidental findings at necropsy or on surgically excised valves and are not associated with cardiac symptoms. This was the case in all 42 tumors in the AFIP series, although three patients had coexisting valvular heart disease (two had chronic rheumatic heart disease and one had luetic aortitis) and three additional patients had severe ischemic heart disease. In at least three reported cases, these tumors were associated with paroxysmal angina pectoris or sudden unexpected death. In these three patients, the papillary tumor was located on the aortic side of the aortic valve and partially obstructed the ostium of a coronary artery.

The patients in this series ranged from 25 to 86 years of age, although 55 percent were older than 60 years. We are aware of only one report of a true papillary fibroelastoma in a child. These lesions are not to be confused with polypoid myxomatous valvular lesions of childhood (incompletely differentiated or dysplastic valves).

Description. Grossly, these tumors resemble a sea anemone, with multiple papillary fronds attached to the endocardium by a short pedicle (fig. 22). Papillary fibroelastomas may arise anywhere in the heart (Table 7), but most frequently arise from the valvular endocardium. When these tumors occur on the atrioventricular valves, they project into the atria. They may arise from the free edge of the valve, but more commonly they arise on the midportion of the valve (pl. I-A). On the semilunar valves, these tumors arise with near equal frequency on the ventricular and arterial side of the valve and may be situated anywhere on the valve (pl. I-B). Occasionally, papillary fibroelastomas are multiple. In three patients in this series, they were multiple and were located on the mitral and aortic valves, the pulmonary and tricuspid valves, and on two cusps of the pulmonary valve.

Histologically and ultrastructurally, the papillary fronds consist of a central core of dense connective tissue surrounded by a layer of loose connective tissue and covered by hyperplastic endocardial cells (fig. 23). The layer of loose connective tissue consists of an acid mucopolysaccharide matrix within which are embedded collagen fibrils, elastic fibers, scattered smooth muscle cells, and occasional mononuclear cells. The amount of elastic tissue is variable, although always present. Usually, a fine meshwork of elastic fibers surrounds the central collagen core (pl. I-C); occasionally, however, the entire central core appears to

TABLE 7

PAPILLARY FIBROELASTOMA
LOCATION IN 42 PATIENTS*

Aortic valve	15
Tricuspid valve	9
Pulmonary valve	8
Mitral valve	7
Right atrium	2
Right ventricle	2
Left ventricular septum	1
Left atrium	1

*The papillary fibroelastoma was located in multiple sites in 3 patients.

Figure 22
PAPILLARY FIBROELASTOMA
Occasionally, papillary fibroelastomas are found on the endocardium away from the valves. They have been reported in all four cardiac chambers. This papillary tumor arose from the endocardium of the right ventricle. The appearance of these papillary tumors has evoked the image of a sea anemone in the minds of many authors. (Courtesy of Dr. J. N. P. Davies, Albany, N. Y.; from Burn, C. G., Bishop, M. B., and Davies, J. N. P. A stalked papillary tumor of the mural endocardium. Am. J. Clin. Pathol. 51:344-346, 1969.)

PLATE I

PAPILLARY FIBROELASTOMA

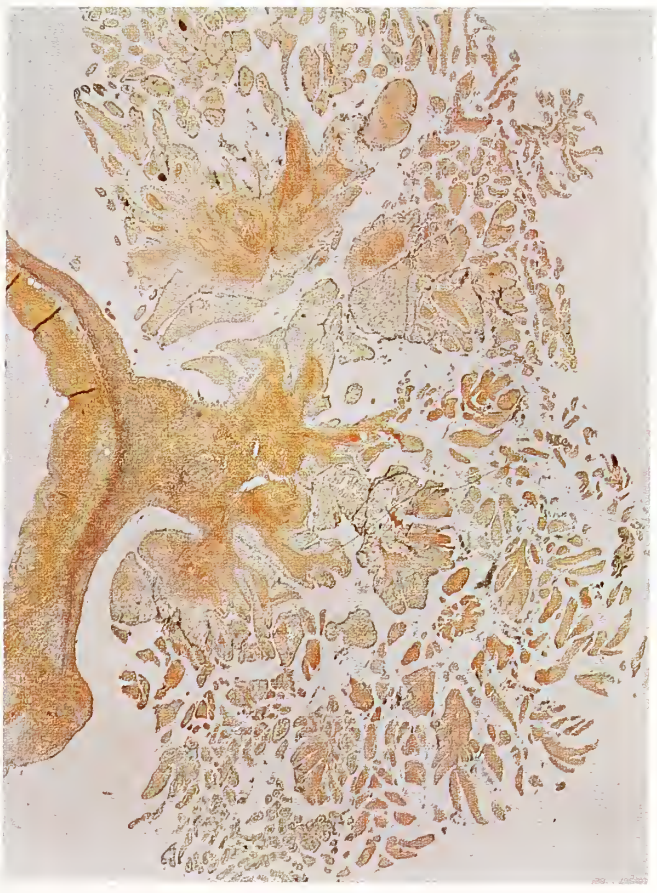
A. Papillary fibroelastomas are primary valvular tumors. On the atrioventricular valves, as on the tricuspid valve illustrated here, they project into the atrial chamber. These tumors consist of multiple papillary fronds arranged on a stalk which merges imperceptibly into the substance of the valve. The fronds consist of a collagen core surrounded by elastic fibers and loose connective tissue. The fronds are covered by endocardial cells. Elastica Van Gieson stain, X16.

B. On the semilunar valves, the papillary fronds frequently project into the arterial lumen; here, a papillary fibroelastoma of the aortic valve projects into the aorta. On the semilunar valves, however, these tumors may project into the ventricular chamber. Movat pentachrome stain, X9.

C. The central collagen core of the papillary fibroelastoma is always surrounded by a dense mesh of elastic fibers. This layer of elastic fibers is a hallmark of this tumor. Surrounding the elastic tissue layer is a variable amount of loose connective tissue, primarily an acid mucopolysaccharide matrix, and the entire frond is then covered by endocardial cells. The structure of the papillary fronds of this tumor closely resembles the structure of normal chordae tendineae. Elastica Van Gieson stain, X175.

PLATE I

A



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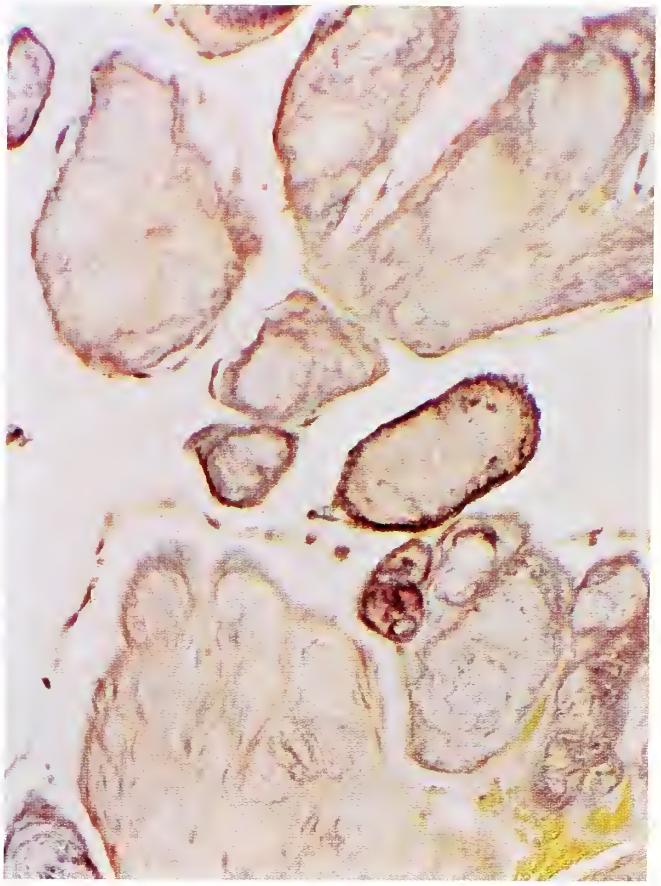

C

consist of elastic fibers. The central core of the papillary fibroelastoma is continuous with the connective tissue of the endocardium, and appears to be a direct extension of the endocardium. Similarly, the hyperplastic endocardial cells covering the papillary fronds merge imperceptibly with the normal endocardial cells.

Whether the papillary fibroelastoma is a true tumor or a hamartoma is debatable. Microscopically, the papillary fronds of these tumors are similar in structure to normal chordae tendineae, and these tumors replicate all the components of normal endocardium. These observations suggest that the papillary fibroelastoma is a hamartoma; however, the fact that these tumors are rarely found in children and are more frequent in older patients, many of whom have longstanding cardiovascular disease, has suggested to other authors that the tumors are secondary to mechanical wear and tear, and represent a degenerative process. Although we also have never seen a papillary fibroelastoma in a child, 21 percent of the patients in the AFIP series were under 50 years of age and had no evidence of cardiovascular disease.

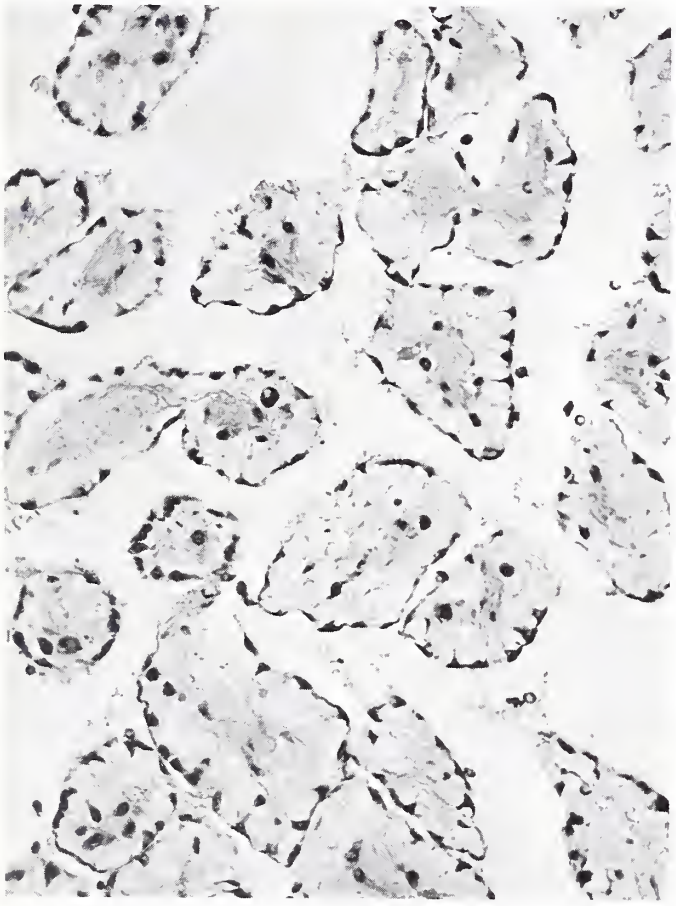

Figure 23
PAPILLARY FIBROELASTOMA

The endocardial cells covering the fronds of the papillary fibroelastoma are in continuity with the endocardial cells covering normal adjacent portions of the valve or endocardium and are structurally identical to these adjacent cells. Focally, especially over the tips of the papillary fronds, the endocardial cells are multilayered and hyperplastic. The loose connective tissue layer surrounding the collagen core is clearly visible at the periphery of the fronds. X225.

These tumors do not represent giant Lambl's excrescences, in our opinion. Lambl's excrescences were reported in 1856 as small filiform tags occurring especially along the contact surfaces of the heart valves. The frequent occurrence of papillary fibroelastomas on the atrial surface of the atrioventricular valves and on the ventricular surface of the semilunar valves parallels the location of Lambl's excrescences; however, Lambl's excrescences do not usually occur on the arterial side of the semilunar valves or on the mural endocardium, whereas papillary fibroelastomas do. Lambl's excrescences are most frequently located along the line of closure of the valves, whereas papillary fibroelastomas are located more frequently on the midportion or body of the valve away from contact surfaces. Lambl's excrescences have been reported in 70 to 85 percent of adult heart valves, whereas papillary fibroelastomas are rare tumors (less than 1 percent of all primary cardiac tumors). Lambl's excrescences are multiple in over 90 percent of the patients, whereas papillary fibroelastomas are rarely multiple (less than 10 percent of our patients). Finally, Lambl's

excrescences, unlike papillary fibroelastomas, contain deposits of fibrin, lack an abundant acid mucopolysaccharide matrix, and do not contain smooth muscle cells.

Treatment. Surgical excision would appear indicated in patients with symptoms of angina pectoris secondary to obstruction of the coronary ostia by the papillary fronds of the papillary fibroelastoma.

Papilloma of the Epicardium

Papillary projections from the epicardium are occasionally seen and are not to be confused with the papillary fibroelastomas of the endocardial surface of the heart. The fronds of the serosal papilloma are composed of loose connective tissue, covered by mesothelial cells, often with a central blood vessel. Unlike the papillary fibroelastoma, they lack a collagen core surrounded by an elastic tissue mantle. The epicardial papillomas are occasionally complex structures with multiple papillary fronds. More frequently, they consist only of one or two fibrous tissue stalks. Histologically, the epicardial papilloma resembles a pericardial adhesion, and focal collections of lymphocytes are frequently seen around the central blood vessels. They most probably represent a localized reactive proliferation of the epicardium, rather than a benign tumor or hamartoma.

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RHABDOMYOMA

SYNONYMS AND RELATED TERMS: Purkinjeoma; congenital glycogenic tumor; rhabdomyomatosis.

Definition. Rhabdomyomas of the heart are almost exclusively tumors of infants and children; in fact, they are the most common primary tumor of the heart in the pediatric age group (less than 15 years old). These tumors are derived from cardiac muscle, are nearly always multiple, and probably represent fetal hamartomas. In approximately one-third of patients, these tumors are associated with tuberous sclerosis.

Clinical Aspects. Clinically, patients with rhabdomyomas can be divided into three distinct groups (Table 8). Group I, approximately one-third of the patients, were either stillborn or died within the first few days of life. Seventy-five percent of these patients had large intracavitary tumors with obstruction of at least one cardiac valve, and presumably the cause of death was secondary to alterations in hemodynamics. Tuberous sclerosis was uncommon in this group; however, establishing the diagnosis of tuberous sclerosis in this age group may be difficult.

TABLE 8

CARDIAC RHABDOMYOMA
CLINICOPATHOLOGIC CORRELATIONS IN 36 PATIENTS*

	Number of Patients	Age Range	Percent Associated Tuberous Sclerosis	Percent Intracavitary Tumors	Percent Cause of Death Related to Rhabdomyoma
Group I	12	SB–18 hrs	25	75	82 †
Group II	11	23 hrs–20 yrs	73	0	0
Group III	13	36 hrs–9 yrs	0	70	77

*Group I=Patients stillborn or dead within 24 hours.
Group II=Patients without clinical cardiac disease.
Group III=Patients with clinical cardiac disease.

†Exact cause of death difficult to determine in this group of patients because 9 of 12 patients were stillborn or died within an hour after birth.

In group II (also approximately one-third of the patients), the majority of the patients had tuberous sclerosis, and the cause of death was primarily related to tuberous sclerosis without major symptoms referable to the heart. The rhabdomyomas were incidental findings at necropsy, and were small and embedded in the myocardium.

Group III were patients who presented with cardiac symptoms: congestive heart failure, cardiac murmurs, arrhythmias, and cardiomegaly. Seventy percent of these patients had intracavitary rhabdomyomas, with marked obstruction to blood flow in at least one cardiac chamber. Interestingly, no patient in Group III had tuberous sclerosis. These patients died either of congestive heart failure or from cardiac arrhythmias.

Description. Grossly, cardiac rhabdomyomas were multiple in 92 percent of patients, varying in size from millimeters to centimeters, and occurring throughout the heart (left ventricle, right ventricle, right atrium, left atrium, epicardium, and endocardium), but never originating from a cardiac valve. Most frequently, rhabdomyomas are located in the myocardium of the left and right ventricles, including the ventricular septum; in at least 50 percent of these patients, a portion of one of the tumors was intracavitary. The tumors are usually white to yellow-tan (figs. 24–26).

Microscopically, the tumors are circumscribed, but not encapsulated and are easily distinguished from the surrounding myofibers. The rhabdomyoma cells are large (up to 80 microns in diameter) and glycogen filled (fig. 27). The histologic demonstration of glycogen is dependent on the speed and types of fixation. Glycogen is best demonstrated with the periodic acid-Schiff reaction (PAS) or with Best's carmine stain on frozen sections from unfixed tissue or following methanol or

nonaqueous fixation. Classic "spider cells," with centrally placed cytoplasmic masses containing the nucleus and elongated projections of slender myofibrils extending to the periphery of the cell, are present in each tumor (figs. 28, 29). More frequently, however, the cytoplasmic mass is eccentrically placed, usually against the cell wall, and the cytoplasmic projections traverse the vacuolated cells. Occasionally, microscopic foci of extramedullary hematopoiesis are prominent.

Ultrastructurally, cellular junctions resembling intercalated disks are located around the total periphery of the rhabdomyoma cells, interconnecting these cells (fig. 30). This ultrastructural feature is unlike normal myocardial cells or Purkinje's cells where intercalated disks are located at the poles of the cell. We do not consider rhabdomyomas abnormal proliferations of specialized (Purkinje cells) or nonspecialized myocardium. Neither is the rhabdomyoma a localized form of glycogen storage disease. In glycogen storage disease with cardiac involvement (Types II, III, and IV), the contractile elements are lost or compressed around the periphery of the cardiac muscle cell by the accumulated glycogen. The cell, however, maintains its

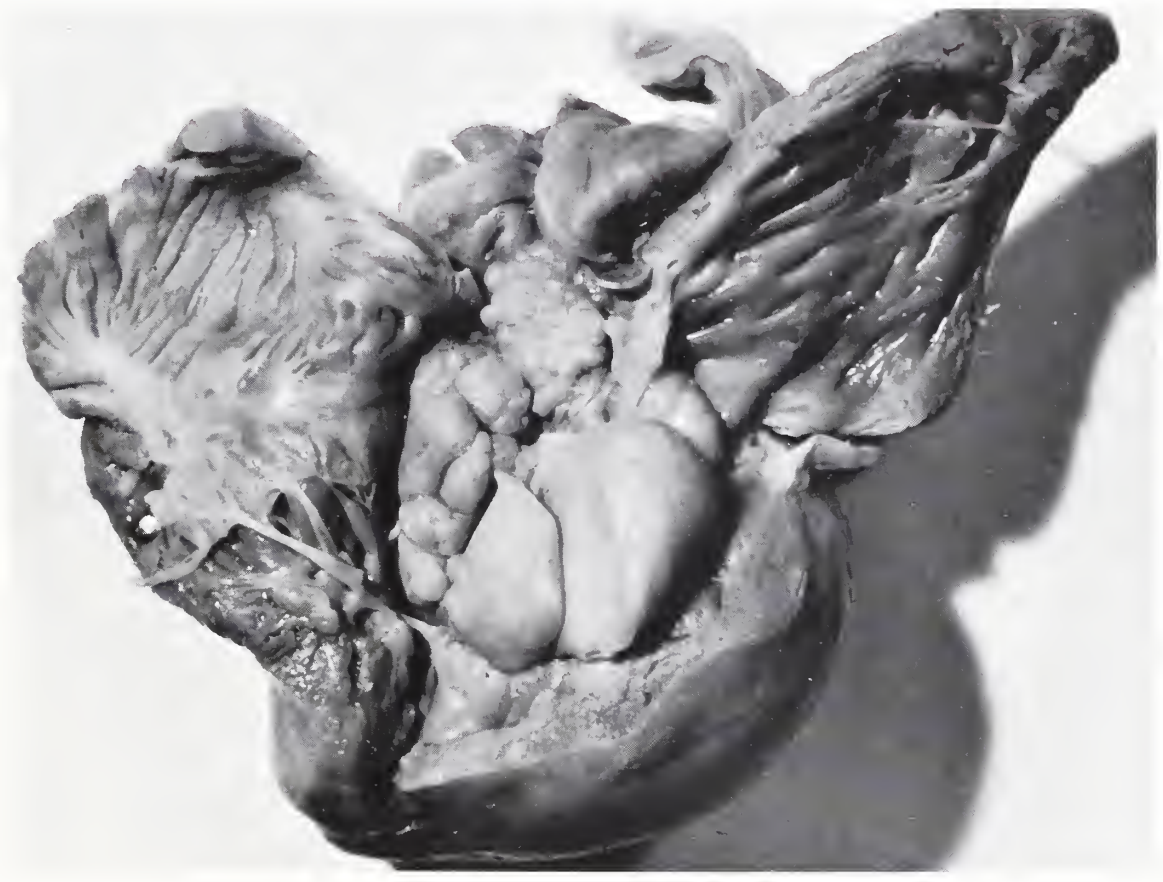

Figure 24
RHABDOMYOMA

This rhabdomyoma fills the right ventricle of a newborn infant and clearly obstructs the tricuspid valve. In approximately 50 percent of children with rhabdomyomas, at least one of the tumors is intracavitary and partially obstructs at least one valve orifice. (See Table 8) (From Fenoglio, J. J., McAllister, H. A., and Ferrans, V. J. Cardiac rhabdomyoma: A clinicopathologic and electron microscopic study. Am. J. Cardiol. 38:241-251, 1976.)

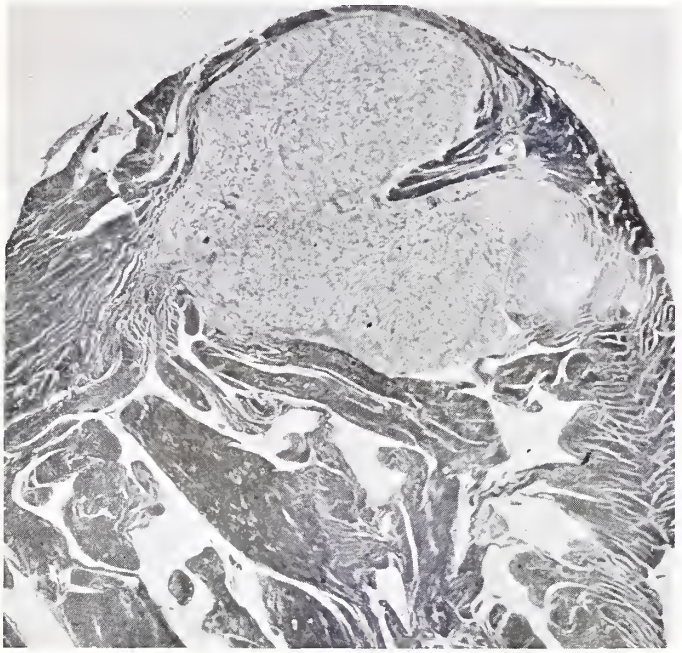

Figure 25
RHABDOMYOMA

The majority of rhabdomyomas are intramyocardial, as illustrated by this tumor in the right ventricular myocardium. Rhabdomyomas occur in all cardiac chambers. Although they are most frequent in the left and right ventricular myocardium, 30 percent occur in the atria. X11.

Figure 26
RHABDOMYOMA

Rhabdomyomas are multiple in over 90 percent of patients and vary in size from millimeters to several centimeters in diameter. Occasionally, multiple, small rhabdomyomas cover either the epicardial surface of the heart, as illustrated, or the endocardial surface.

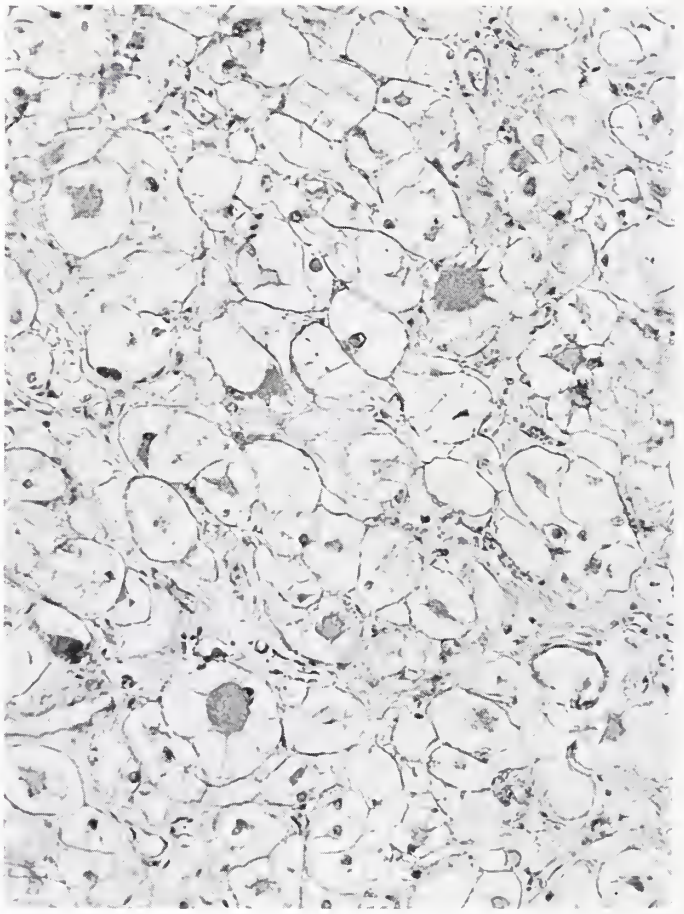

Figure 27
RHABDOMYOMA
(Figures 27 and 28 from same case)

Rhabdomyomas are composed of vacuolated, large, ovoid cells. Islands and strands of cytoplasm are seen against the cell membrane and, occasionally, in the center of the cell. If the tissue is fixed in methyl alcohol, the vacuolated areas in the formaldehyde fixed tissue are easily demonstrated to contain abundant glycogen. X125.

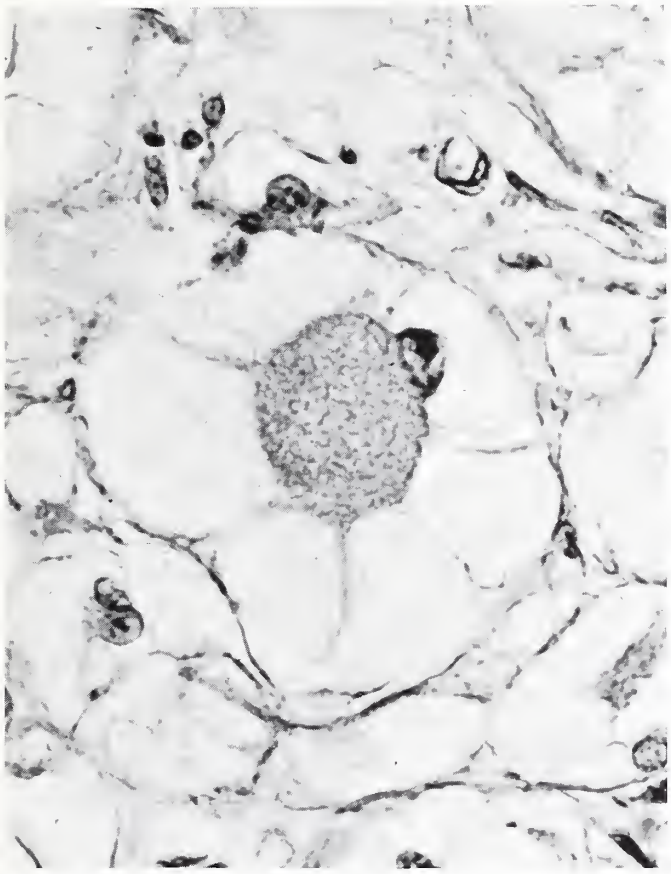

Figure 28
RHABDOMYOMA

The spider cell, with a central cytoplasmic mass and strands of cytoplasm that extend to the cell membrane, is pathognomonic of the rhabdomyoma (fig. 27). Although often not abundant, they can be found in every rhabdomyoma. The nucleus is usually centrally located, but may be eccentrically placed as in this cell. The vacuoles here, clearly separated by strands of cytoplasm, contain glycogen which has been leached from the cell during fixation. X525.

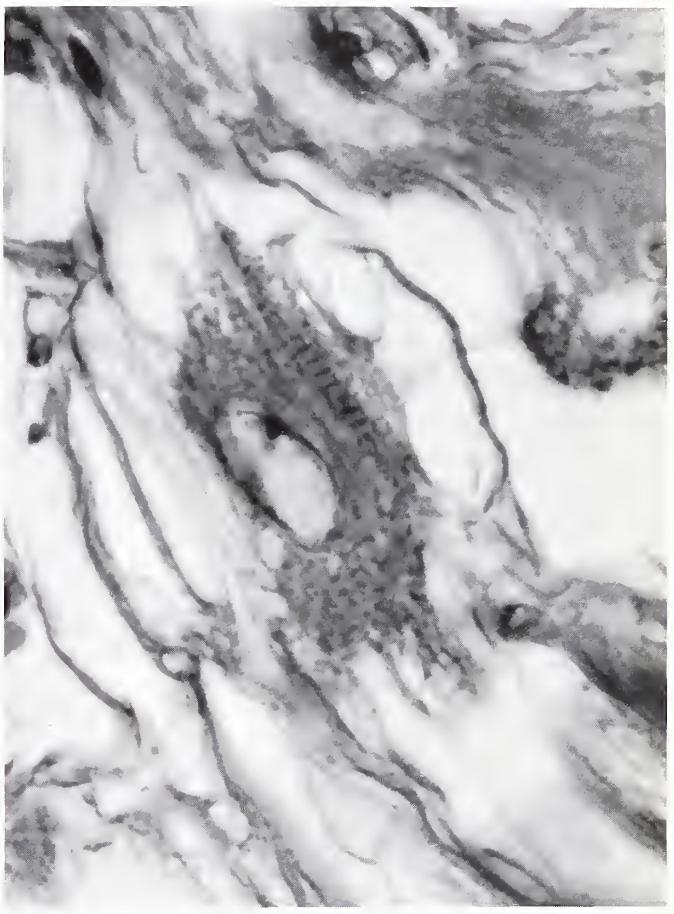

Figure 29
RHABDOMYOMA

If carefully searched for, bundles of myofilaments with distinct cross-striations (Z bands) can be identified in the cytoplasmic masses and strands of the rhabdomyoma cell. The findings of myofibrils convincingly establishes the diagnosis of rhabdomyoma. X890.

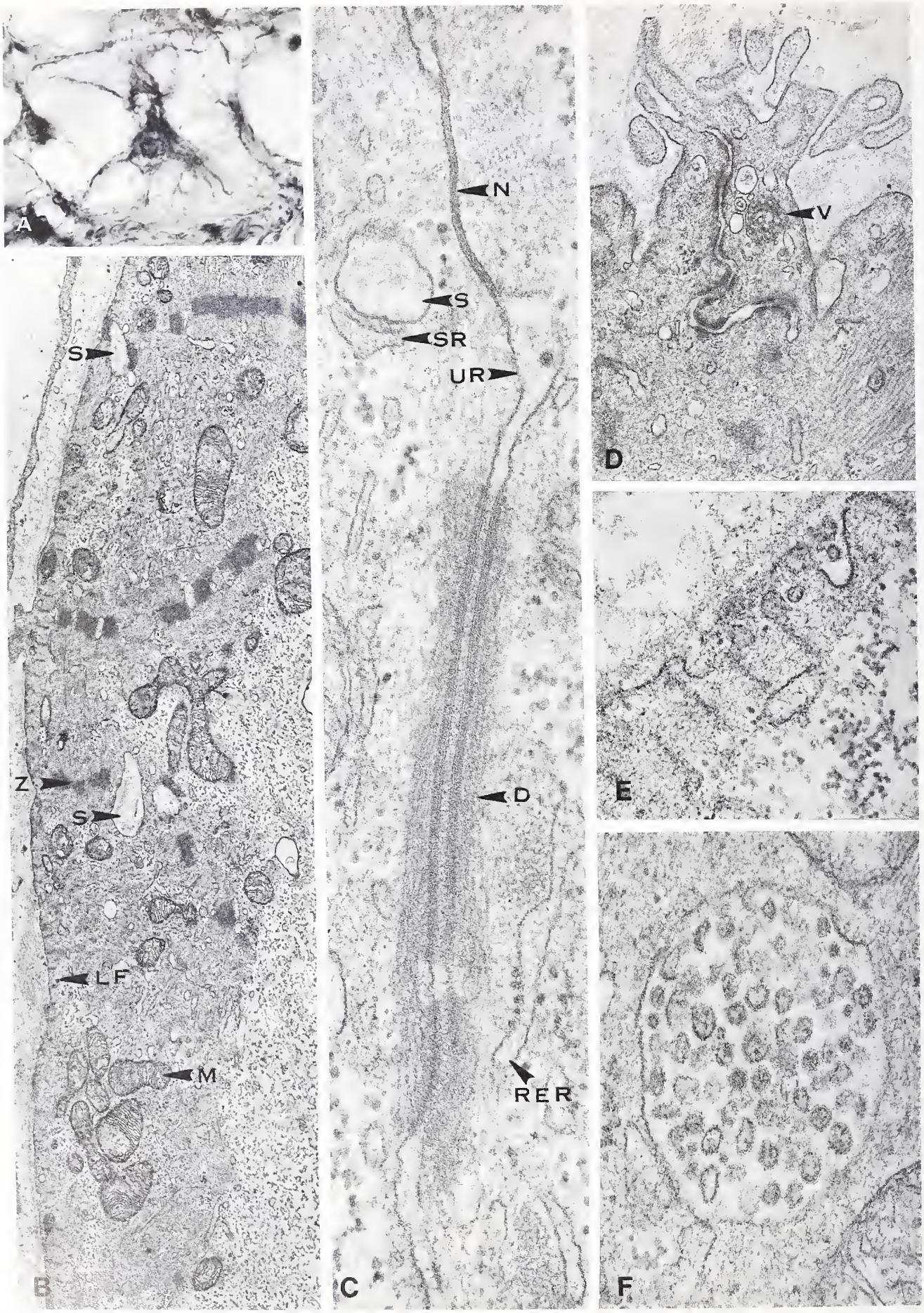

Figure 30

cylindrical shape and intercalated disks are located at the two poles of the cell. The preservation of a relatively normal cell shape distinguishes glycogen-laden cardiac muscle cells in glycogen storage disease from rhabdomyoma cells. The ovoid shape and the peripheral location of cellular junctions of intercalated disk type in rhabdomyoma cells are reminiscent of cardiac myoblasts. This suggests that the tumor is a fetal hamartoma derived from embryonic cardiac myoblasts.

Differential diagnosis from granular cell tumor, rhabdomyoma, fibroma, and lipoma may be difficult. Differentiating characteristics of these tumors will be discussed in their appropriate chapters.

Treatment. Cardiac rhabdomyomas have been successfully excised in at least five patients. All these patients had intracavitary rhabdomyomas and cardiac symptoms. Since there is no evidence to suggest that rhabdomyoma cells are capable of mitotic division after birth, and tuberous sclerosis appears to be rare in patients with intracavitary rhabdomyomas and cardiac symptoms, we suggest that this group of patients (Group III) may be amenable to surgical treatment.

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Figure 30
RHABDOMYOMA

Histology of rhabdomyoma cells and ultrastructure of their surfaces.

A. This histologic section of a typical rhabdomyoma cell (spider cell) has a centrally located nucleus and surrounding cytoplasmic mass with radial extensions. X400.

B. The free surface of a rhabdomyoma cell is invested by a thin layer of basal lamina. Sarcolemmal invaginations (S) also are lined by basal lamina and are located close to Z bands (Z) of peripheral myofibrils. Leptofibrils (LF) are immediately subjacent to the sarcolemma. Mitochondria (M) are small and sparse; glycogen particles occupy myofibril-free areas of the cell. X15,600.

C. A nexus (N), a desmosome (D), and an undifferentiated region (UR) form part of the intercellular junction. A sarcolemmal invagination (S) and a closely apposed cistern of sarcoplasmic reticulum (SR), filled with fine, moderately dense granules (SR), are located near the surface of one cell. Both cells contain scattered elements of SR, one of which (RER) has ribosomes attached to its outer surface. X80,175.

D. This small protrusion of the surface of a rhabdomyoma cell bears intracytoplasmic junction formed by the apposition of two parts of the plasma membrane of the same cell. A small vesicle (V) containing spherical microparticles is seen to the right of this junction. X30,500.

E. This high magnification view shows leptofibrils, which are composed of dense bands alternating with arrays of thin filaments. X53,200.

F. A vesicle similar to that in D is limited by a single, trilaminar membrane and is filled with spherical microparticles. X68,200.

(From Fenoglio, J. J., Diana, D. J., Bowen, T. E., McAllister, H. A., and Ferrans, V. J. Ultrastructure of a cardiac rhabdomyoma. Hum. Pathol. 8:700-706, 1977.)

FIBROMA

SYNONYMS AND RELATED TERMS: Rhabdomyofibroma; congenital mesoblastic tumor; fibrous hamartoma.

Definition. Fibromas of the heart are connective tissue tumors derived from fibroblasts and have the same spectrum of appearance and behavior as the soft tissue fibromatoses described in the fascicle "Tumors of the Soft Tissues." Cardiac fibromas are definable masses of proliferating connective tissue and are not to be confused with reactive fibrous tissue proliferations on the endocardial or epicardial surfaces of the heart. These tumors occur at all ages and in both sexes, although they are more frequent in children, and, as such, are the second most common primary cardiac tumor in the pediatric age group.

Clinical Aspects. The clinical findings in 17 patients with fibromas were dependent on the location of the tumor, as summarized in Table 9. Ten fibromas of the ventricular septum were inoperable, and the patients either died suddenly or developed intractable congestive heart failure. The majority of these tumors encroached on, or invaded the conduction system, usually the left and right bundle branches, and the patients either developed ventricular fibrillation or died suddenly and unexpectedly. Seven patients with fibromas located in the ventricular free wall or atrium presented with cardiomegaly, usually as an incidental finding on a routine chest x-ray. The mass lesion was defined by cardiac catheterization, and surgical excision was attempted in five patients. One patient died but four were alive and well, without evidence of recurrence, at least two years following operation.

Description. Fibromas are almost always single and located in the ventricular myocardium, frequently in the ventricular septum (pl. II-A). These firm, gray-white tumors are often large and sometimes exceed 10 cm. in diameter; they interdigitate with the surrounding myocardium. Central calcification is frequent and often may be seen on chest roentgenograms. Microscopically, these tumors are nonencapsulated and extend into the surrounding myocardium (pl. II-B). There may be the impression of satellite nodules, but, in fact, these nodules connect to the main tumor mass at a different plane. Central portions of the tumor are composed of hyalinized fibrous tissue, often with multiple foci of calcification and cystic degeneration. Fibromatoses, by definition, have a poor blood supply, as evidenced by the paucity of capillaries, and, therefore, it is not surprising to find central areas of cystic degeneration and dystrophic calcification (fig. 31). Elastic tissue may also be prominent as in many of the fibromatoses of the superficial soft tissues. Areas of cellular fibrous tissue are present in each tumor, usually around the periphery (pl. III-A); however, in the largest tumors, these areas are less frequent. Mitotic figures are rare in these areas of cellular fibrous tissue, and, as in the extracardiac fibromatoses, cellularity is not an indication of malignancy (pl. III-B). We are not aware of any bonafide metastasis from a true fibroma of the heart. Because of the expansile growth of these tumors, normal cardiac muscle cells are frequently entrapped in the growing fibrous tissue and are left intact deep within the tumor, often in central locations. These cells degenerate and become vacuolated as they are cut off from the contracting myocardium; this has led pathologists to speculate that the fibroma is a "healing

TABLE 9

CARDIAC FIBROMA
CLINICOPATHOLOGIC CORRELATIONS IN 17 PATIENTS

Case Number	Age	Sex	Clinical Findings: Murmurs	Arrhythmias	Respiratory Findings	X-ray Findings	Catheterization Data	Autopsy Findings: Site	Number	Size	Calcium	Conduction System	Operative Findings	Cause of Death
GROUP I – 10 PATIENTS WITH FIBROMA OF THE VENTRICULAR SEPTUM														
1	7wks	F	Systolic	Ventricular fibrillation	0	Cardiomegaly	0	Septum	1	5cm	0	Compression	Inoperable	Ventricular fibrillation
2	8wks	F	Systolic I/VI	0	0	Cardiomegaly	Mass lesion	Septum	1	4cm	0	0	Inoperable	Congestive heart failure
3	3mos	F	0	0	0	0	0	Septum	1	4.5cm	0	Compression		Sudden unexpected death
4	35mos	F	0	0	0	0	0	Septum l. vent.	4	>4cm	0	Invasion		Sudden unexpected death
5	5mos	F	0	0	0	0	0	Septum	1	4cm	0	Compression		Sudden unexpected death
6	9mos	F	Systolic III/VI	0	0	Cardiomegaly	Mass lesion	Septum	1	8cm	0	0	Inoperable	Congestive heart failure
7	17mos	F	0	0	0	0	0	Septum	1	8cm	+	Compression		Sudden unexpected death
8	4½yrs	M	0	0	Pneumonia	Cardiomegaly	0	Septum	1	5cm	0	Compression		Sudden unexpected death
9	39yrs	M	0	0	0	0	0	Septum	1	6cm	0	Compression		Sudden unexpected death
10	56yrs	M	Systolic II/VI	Ventricular fibrillation	0	Cardiomegaly	Mass lesion	Septum	1	7cm	+	Compression	Inoperable	Ventricular fibrillation
GROUP II – 7 PATIENTS WITH FIBROMA OF THE VENTRICULAR FREE WALL AND ATRIUM														
11	17mos	M	0	0	Pneumonia	Mediastinal mass	0	Left	1	10cm	+	0	Excision	
12	18mos	M	0	0	Edema	Cardiomegaly	0	Right	1	7cm	+	0		Obstruction of tricuspid valve
13	4yrs	M	Systolic I/VI	0	0	Cardiomegaly	Mass lesion	Left	1	6cm	0	0	Excision	
14	12yrs	M	0	0	0	Cardiomegaly	Extracardiac mass	Apex	1	5cm	0	0	Excision	
15	17yrs	F	Systolic II/VI	0	0	Cardiomegaly	Mass lesion	Apex	1	5cm	+	0	Excision	
16	18yrs	F	0	0	0	Cardiomegaly	Mass lesion	Apex	1	6cm	0	0	Excision	
17	47yrs	M	0	0	0	0	0	Right atrium	1	3cm	0	0		Incidental finding

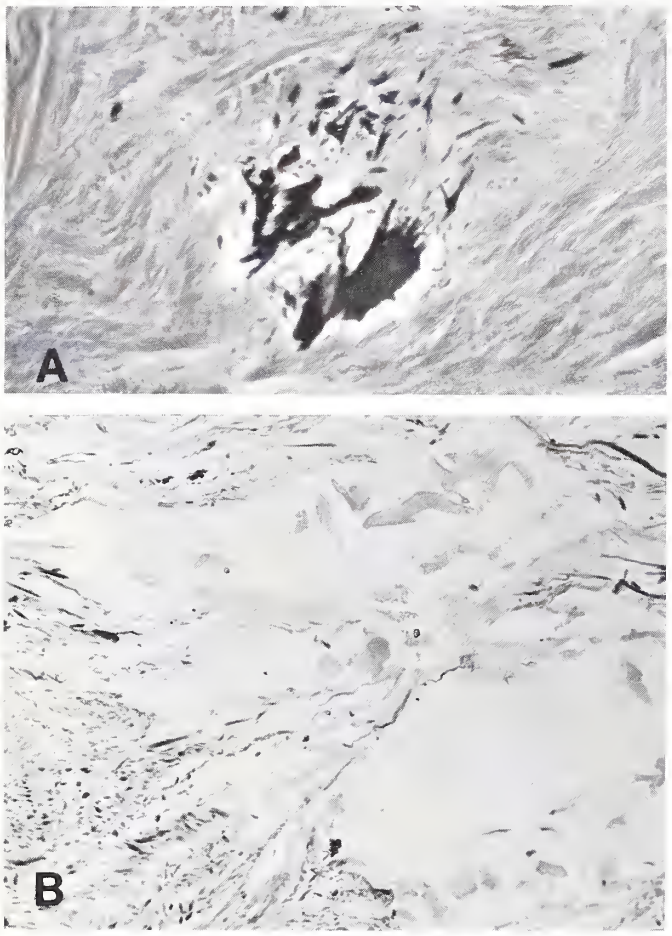

Figure 31
FIBROMA
(Figure 31 and Plate II-B from same case)

A. Microscopic as well as macroscopic foci of calcification are frequent in fibromas and often make sectioning difficult. X150.

B. In addition, areas of cystic degeneration are frequent in the central portions of the larger tumors. X50.

Both findings are secondary to the poor blood supply in fibrous tumors.

rhabdomyoma" or a "mesoblastic tumor." In fact, by both light and electron microscopy, these are degenerating cardiac muscle cells, not embryonic (rhabdomyoma) muscle cells, and are not part of the fibroma. True "spider cells"—diagnostic of a rhabdomyoma—are not found in the cardiac fibroma.

Treatment. Tumors located outside the ventricular septum are amenable to surgical excision, and these patients usually do well following surgery. Surgical resection of ventricular septal fibromas may not be possible, especially if the tumor is close to the conduction system; such patients often succumb to ventricular arrythmias. The efficacy of permanent cardiac pacing in patients with large ventricular septal fibromas has not been adequately evaluated.

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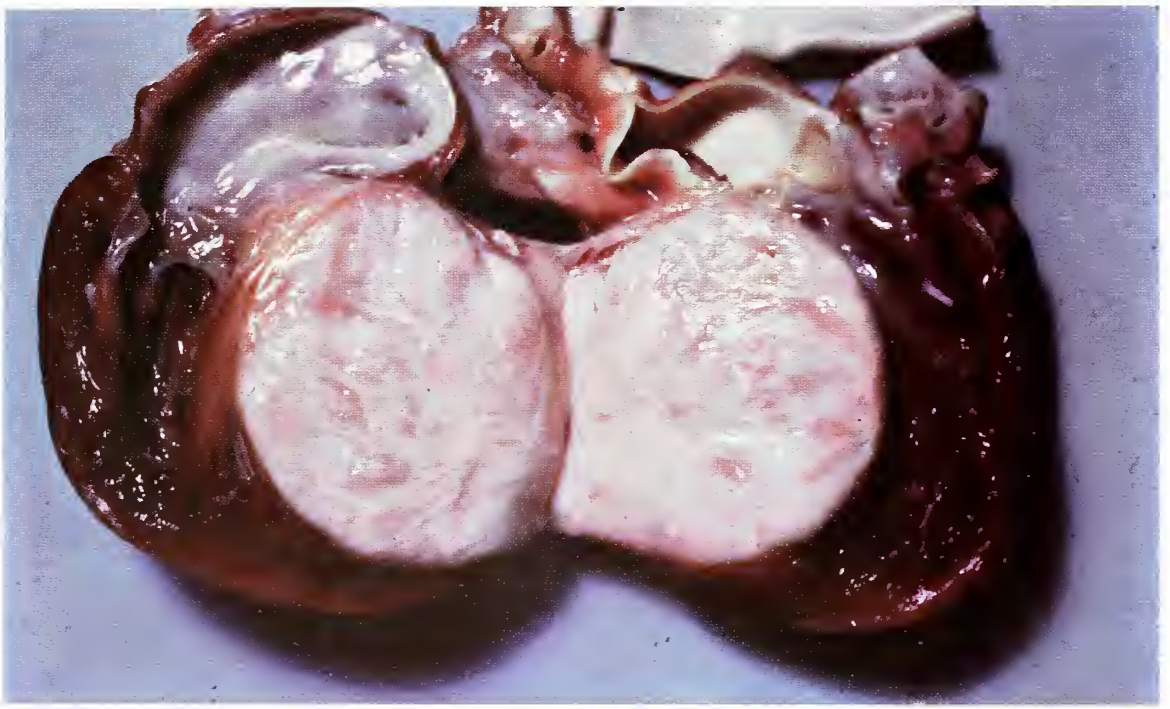
PLATE II

FIBROMA
(Plate II-B and Figure 31 from same case)

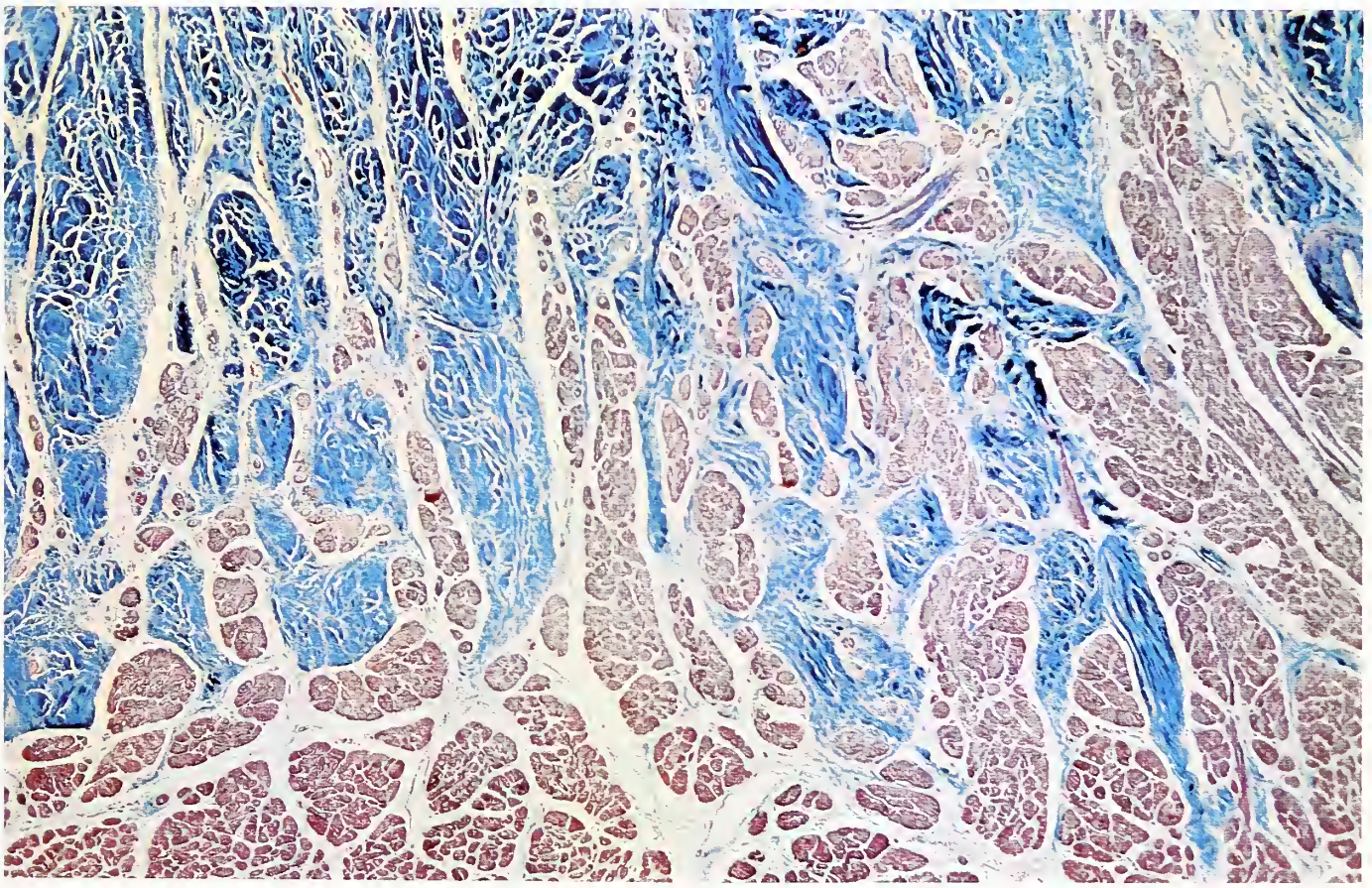
A. Fibromas are most frequently located in the ventricular septum, are usually single, and often reach massive proportion. This fibroma completely replaced the ventricular septum and encroached upon the left ventricular chamber. On cross section, the tumors are firm and appear trabeculated. Foci of calcification and areas of cystic degeneration are frequently apparent grossly.

B. Although grossly fibromas appear encapsulated, microscopically they merge and interdigitate with the surrounding myocardium. A large percentage of the tumor mass is composed of dense, acellular collagen which often appears hyalinized. Masson's trichrome stain, X50.

PLATE II



A



B

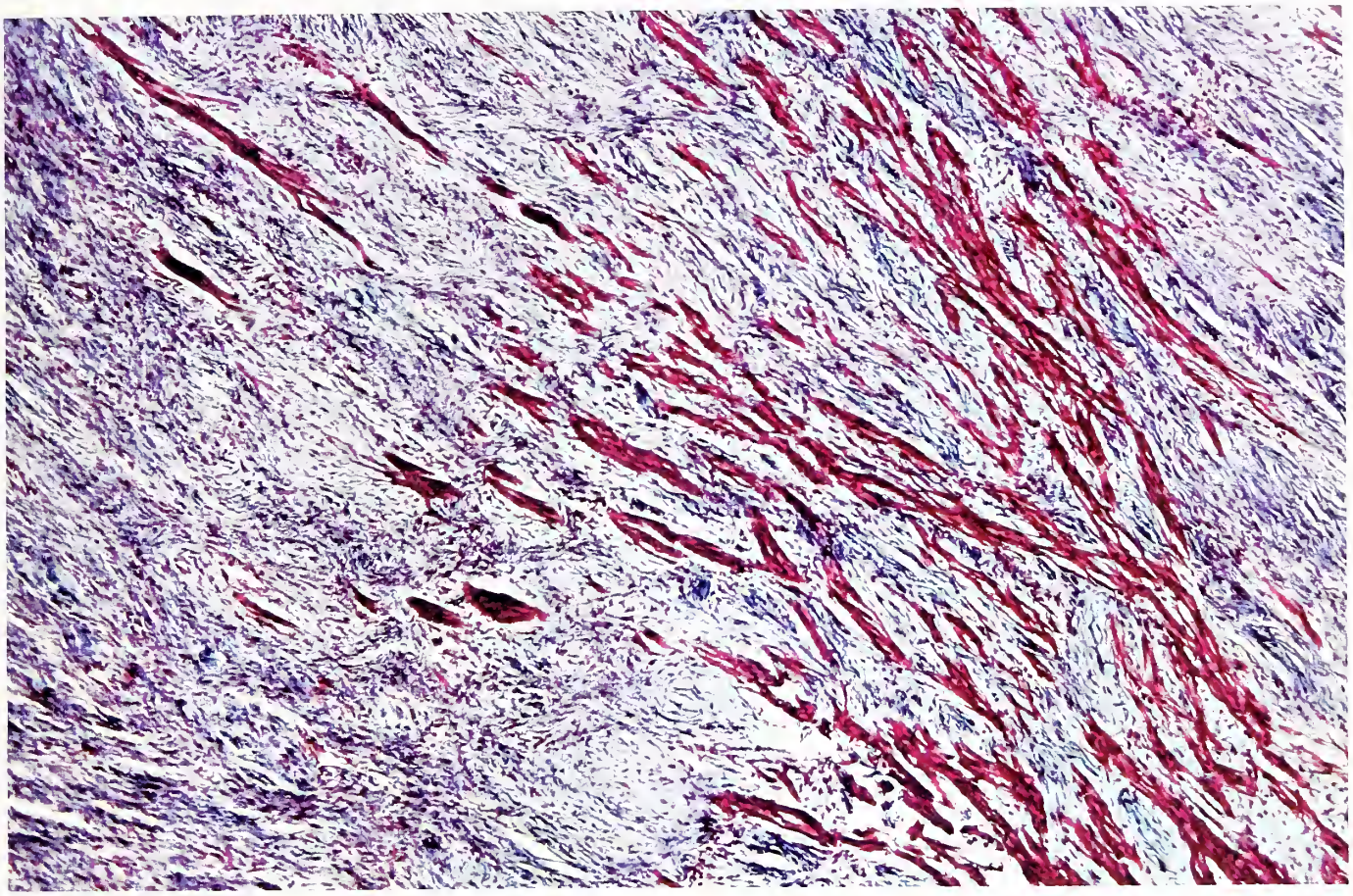
PLATE III

FIBROMA

A. Foci of cellular fibrous tissue are found in every fibroma, usually around the periphery of, but also within the tumor mass. Bundles of, as well as individual myofibers are entrapped in the expanding fibrous tissue and are often found deep within the fibroma. These are normal, although often degenerating myofibers as illustrated by the deeply red staining cells in the photomicrograph. These cells are **not** rhabdomyoblasts, and do **not** arise from the replicating cells of the fibroma. Masson's trichrome stain, X50.

B. The cellular areas of the fibroma consist of spindle-shaped cells with blunt-ended nuclei and abundant cytoplasm. There is often a moderate degree of nuclear atypia; however, mitotic figures are distinctly unusual. Extracellular collagen is abundant, but blood vessels and capillaries are relatively lacking. This morphologic pattern is strikingly similar to that of the fibromatoses of soft tissues. Masson's trichrome stain, X485.

PLATE III



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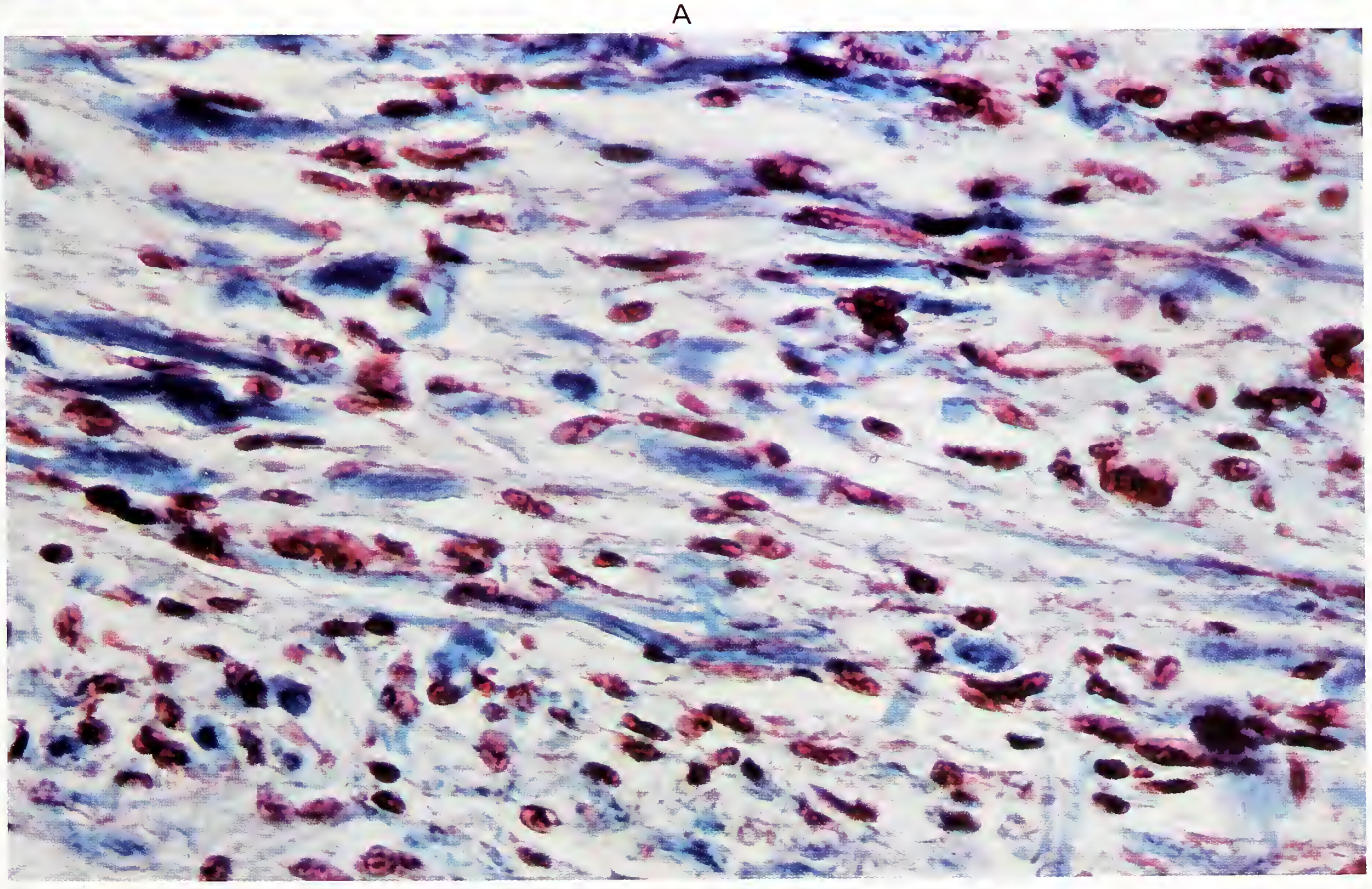

B

LIPOMATOUS HYPERTROPHY OF THE ATRIAL SEPTUM AND LIPOMA

SYNONYMS AND RELATED TERMS: Rhabdomyolipoma; fibrolipoma; fatty hamartoma; interatrial lipoma.

Definition. Lipomatous hypertrophy of the atrial septum and cardiac lipomas are characterized by abnormal accumulations of adipose tissue forming a recognizable mass. These masses may contain entrapped cardiac muscle cells, abundant fibrous tissue, multiple blood vessels, and fetal fat cells; however, their principal component is mature adipose tissue.

The clinical and pathologic findings in 45 patients with abnormal accumulations of adipose tissue in the heart and pericardium are summarized in Tables 10 and 11. The series has been divided into two groups: lipomatous hypertrophy of the atrial septum and true lipomas or lipomas that are encapsulated or surrounded by cardiac muscle. Lipomatous hypertrophy is a nonencapsulated mass of adipose tissue in the atrial septum that is in continuity with the epicardial fat. It most probably represents atypical hyperplasia of primordial fat rather than a true tumor.

Lipomatous Hypertrophy of the Atrial Septum (Interatrial Lipoma)

Clinical Aspects. These tumors may be associated with cardiac symptoms, especially cardiac arrhythmias (see Table 10). In 28 percent of the patients in our series, the cause of death appears directly related to the atrial tumor. These patients (1, 3–6, 11, 17, 26, 31) died either suddenly or following prolonged episodes of atrial or ventricular arrhythmia or intractable congestive heart failure. The etiology of the cardiac symptomatology was unclear clinically in each case, and at necropsy no abnormality or cardiac disease other than lipomatous hypertrophy of the atrial septum was found. In two additional patients (13, 19), the conduction disturbances appeared directly related to the mass in the atrial septum, although the demise of these patients cannot be attributed to the interatrial lipoma. Of the remaining 21 patients, 11 had either conduction disturbances or evidence of congestive heart failure; however, in each case, the relationship of these findings to coexistent cardiopulmonary disease was unclear. In 10 patients, the lipomatous hypertrophy was an incidental finding at autopsy. Cross-sectional echocardiography should be helpful in defining this condition. The clue to the presence of lipomatous hypertrophy is intractable congestive heart failure, or persistent rhythm disturbances in the absence of a clinically definable etiology.

Ten patients in this series had either chronic or debilitating diseases; however, this did not correlate with the size of the interatrial lipoma or with the presence of rhythm disturbance. Similarly, the body habitus of the patient and the amount of epicardial fat did not correlate with the size of the interatrial lipoma or with the rhythm disturbances.

Although the majority of patients with lipomatous hypertrophy of the atrial septum are over 60 years of age, approximately 25 percent of the patients in our series are younger, and we have seen lipomatous hypertrophy of the atrial septum in a 22 year old man.

TABLE 10

LIPOMATOUS HYPERTROPHY OF THE ATRIAL SEPTUM
CLINICOPATHOLOGIC CORRELATIONS IN 32 PATIENTS

Patient	Age	Sex	Site	Cardiac Symptoms	Duration	Pathology
1	22 yrs	M	Atrial septum	None		Sudden unexpected death
2	49 yrs	M	Atrial septum	None		Pneumonia, acute
3	52 yrs	M	Atrial septum	Atrial fibrillation	4 yrs	Ventricular fibrillation
4	53 yrs	M	Atrial septum	Atrial fibrillation/ congestive heart failure	4 yrs	Sudden death
5	53 yrs	F	Atrial septum	Dyspnea/congestive heart failure	6 mos	Sudden death
6	54 yrs	F	Atrial septum	Congestive heart failure/ tachycardia	7mos	Intractable congestive heart failure
7	55 yrs	M	Atrial septum	None		Chlorpromazine intoxication
8	57 yrs	M	Atrial septum	None		Perforated gastric ulcer
9	62 yrs	M	Atrial septum	Idioventricular rhythm	1 yr	Emphysema, cor pulmonale
10	64 yrs	F	Atrial septum	None		Bronchogenic carcinoma with metastasis
11	64 yrs	M	Atrial septum	Congestive heart failure/ syncope/premature ventricular contractions	2 yrs	Pulmonary edema
12	66 yrs	M	Atrial septum	Angina/myocardial infarct		Lipoma incidental finding at time of coronary bypass surgery
13	66 yrs	M	Atrial septum	Dyspnea/congestive heart failure/atrial flutter	2 yrs	Intractable congestive heart failure, digitalis toxicity
14	67 yrs	M	Atrial septum	None		Small bowel infarct
15	57 yrs	M	Atrial septum	Premature atrial contractions/ sinus tachycardia	3 yrs	Emphysema, cor pulmonale
16	68 yrs	M	Atrial septum	None		Myocarditis, sudden unexpected death
17	68 yrs	M	Atrial septum	Primary atrioventricular block/ Atrial fibrillation	2 yrs	Cardiac arrest following abdominal surgery
18	68 yrs	M	Atrial septum	Congestive heart failure/ hypertension	2 yrs	Refractory congestive heart failure
19	69 yrs	M	Atrial septum	Right bundle branch block/ premature contractions	?	Squamous cell carcinoma with metastasis
20	70 yrs	F	Atrial septum	Sinus tachycardia/premature atrial contractions/hypertension/cardiomegaly	5 yrs	Atherosclerotic heart disease, cerebrovascular accident, old
21	71 yrs	F	Atrial septum	None		Cerebrovascular accident
22	72 yrs	M	Atrial septum	None		Carcinoma of prostate
23	72 yrs	M	Atrial septum	None		Salmonella enterocolitis
24	73 yrs	F	Atrial septum	Congestive heart failure/ atrial fibrillation	1 yr	Intractable congestive heart failure, aortic stenosis
25	75 yrs	M	Atrial septum	Premature atrial contractions	?	Myocardial infarct, acute emphysema, cor pulmonale
26	78 yrs	F	Atrial septum	Congestive heart failure	2 yrs	Intractable congestive heart failure
27	79 yrs	F	Atrial septum	Variable primary atrioventricular block/congestive heart failure	1 mos	Digitalis toxicity
28	80 yrs	M	Atrial septum	Cardiomegaly/congestive heart failure	years	Emphysema, cor pulmonale
29	81 yrs	M	Atrial septum	None		Intratrochanteric fracture
30	83 yrs	F	Atrial septum	Atrial fibrillation/congestive heart failure	years	Mitral and aortic stenosis, pulmonary emboli
31	87 yrs	M	Atrial septum	Premature atrial tachycardia/ atrial fibrillation/congestive heart failure	4 yrs	Perforated gastric ulcer
32	88 yrs	F	Atrial septum	Premature atrial and ventricular contractions	2 mos	Hyperthyroidism, medullary carcinoma thyroid

Figure 32
LIPOMATOUS HYPERTROPHY OF ATRIAL SEPTUM
The mass is confined to the atrial septum and grossly distorts and thickens the septum, often in a uniform fashion—hence, the designation lipomatous hypertrophy of the atrial septum. Grossly, the septum is clearly infiltrated by yellow-gray adipose tissue.

Figure 33
LIPOMATOUS HYPERTROPHY OF ATRIAL SEPTUM
Occasionally, a portion of the tumor projects into the atrial cavity, usually the right atrium. The intracavitary portion of the tumor may be large enough to be detected by angiography and mistakenly interpreted as a myxoma. The abnormal accumulation of lipid usually impinges upon the region of the atrioventricular node, which lies just above the septal leaflet of the tricuspid valve, near the junction of the septal leaflet with the anterior leaflet. The intracavitary portion of this tumor is situated just above the region of the atrioventricular node.

Description. The mass is located in the atrial septum, and grossly bulges from beneath the atrial endocardium, most frequently into the right atrium (fig. 32). Occasionally, a lipomatous hypertrophy of the atrial septum may protrude so far into the atrium that this entity must be considered in the angiographic differential diagnosis of intracavitary atrial masses (fig. 33). These tumors vary in size from 1 or 2 cm. up to 7 or 8 cm. in maximum diameter. They may extend into the region of the atrioventricular node (fig. 34), but most often are located anterior to the foramen ovale. The lipoma of the atrial septum is situated in the area of at least two proposed intra-atrial conduction pathways. It is not known whether this is the reason for the rhythm disturbances in these patients or what effect it will have on medical management. The mass is nonencapsulated, but apparently circumscribed, and differs in color and consistency from the epicardial fat. Interatrial lipomas are usually brown-tinged and firm.

Microscopically, they consist of varying proportions of mature adipose tissue and granular and/or vacuolated cells (fig. 35). Fat droplets are usually demonstrable both in the mature fat cells and in the granular cells with oil red O stains. By both light and electron microscopy, the granular cells are identical to fetal fat cells. The presence of fetal fat is a hallmark of lipomatous hypertrophy of the atrial septum and, occasionally, these interatrial masses consist almost entirely of fetal fat. Myocardial cells are invariably entrapped in the mass,

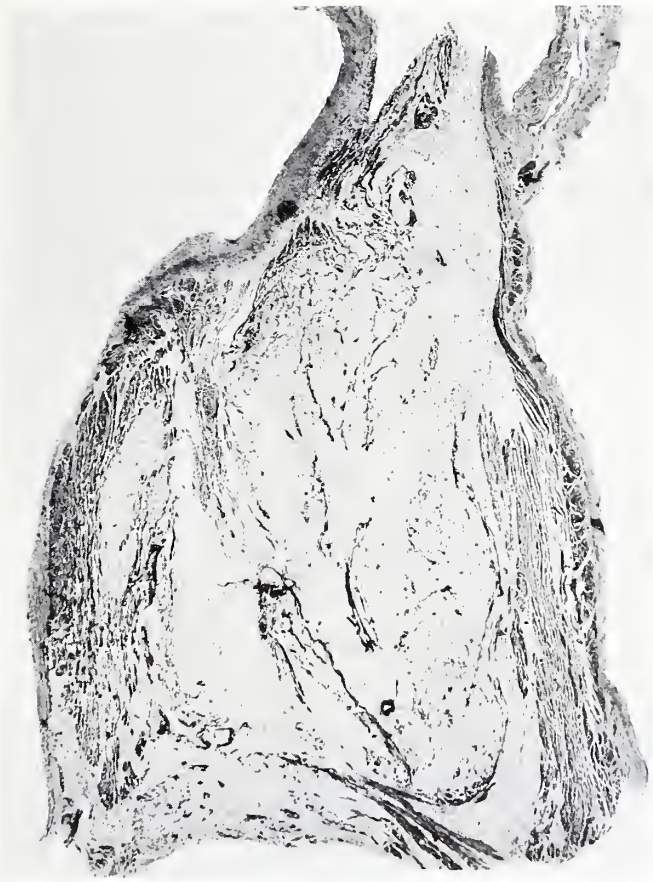

Figure 34
LIPOMATOUS HYPERTROPHY OF ATRIAL SEPTUM

The atrial septum is thickened by adipose tissue, and the myofibers are compressed against the endocardium. Islands of atrial myofibers are trapped in the lipoma and often do not appear to be in contact with the myofibers compressed against the endocardium. Blood vessels and fibrous tissue septae are abundant. X8.

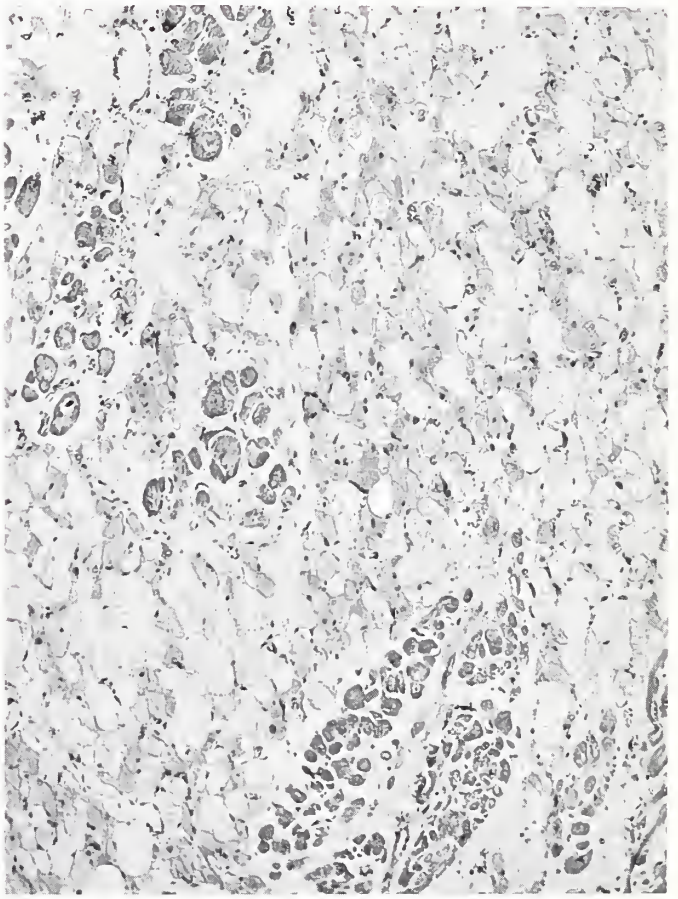

Figure 35
LIPOMATOUS HYPERTROPHY OF ATRIAL SEPTUM

Lipomatous hypertrophy of the atrial septum is composed of mature adipose tissue and varying amounts of fetal fat, represented by the gray, granular appearing cells. Fetal fat is a hallmark and is present in varying proportions in every instance. Trapped in the adipose tissue are bundles of atrial myofibers, many of which are vacuolated and appear to be degenerating. X70.

especially at the periphery (fig. 34). Many of the entrapped myocardial cells demonstrate bizarre hypertrophic, atrophic, or degenerative changes. Often the muscle nuclei are large, hyper-chromatic, and pleomorphic—changes consistent with cellular hypertrophy. Classic "spider cells" or neoplastic muscle cells are never found in the interatrial lipoma. Varying amounts of replacement fibrosis and foci of chronic inflammatory cells, predominantly lymphocytes and plasma cells, are frequently present.

Treatment. The arrhythmias secondary to lipomatous hypertrophy of the atrial septum should be amenable to medical management. The use of cardiac pacing has been advocated.

Lipoma (Exclusive of Lipomatous Hypertrophy of the Atrial Septum)

Clinical Aspects. True lipomas are less frequent than lipomatous hypertrophy of the atrial septum (interatrial lipomas) and occur throughout the heart, including the visceral and parietal pericardium (Table 11). The tumors in this series were usually not associated with cardiac symptoms unless situated in the visceral or parietal pericardium or projecting into the pericardial sac. Parietal pericardial lipomas are often mistaken clinically for pericardial cysts, and visceral pericardial lipomas are frequently associated with a pericardial effusion. Relief of symptoms follows surgical excision of both the visceral and parietal pericardial lipomas.

Description. True lipomas are encapsulated masses of adult adipose tissue. When located within the myocardium, they are usually small, irregular in contour, and have a barely definable, but definite capsule (fig. 36). The pericardial and cavitary lipomas are bosselated and may reach 10 cm. or more in diameter. Grossly, they are identical in appearance to adult fat or lipomas elsewhere in the body.

Microscopically, they consist of mature fat cells with varying amounts of fibrous tissue, myxoid tissue, and blood vessels, identical to the histologic spectrum seen in soft tissue lipomas (fig. 37). Rarely, fetal fat cells are present. When lipomas occur in the myocardium, varying numbers of myocardial cells are invariably entrapped in the tumor. Three lipomas (25 percent in the AFIP series) were multiple, and each patient had tuberous sclerosis. These lipomas had abundant cardiac muscle en-

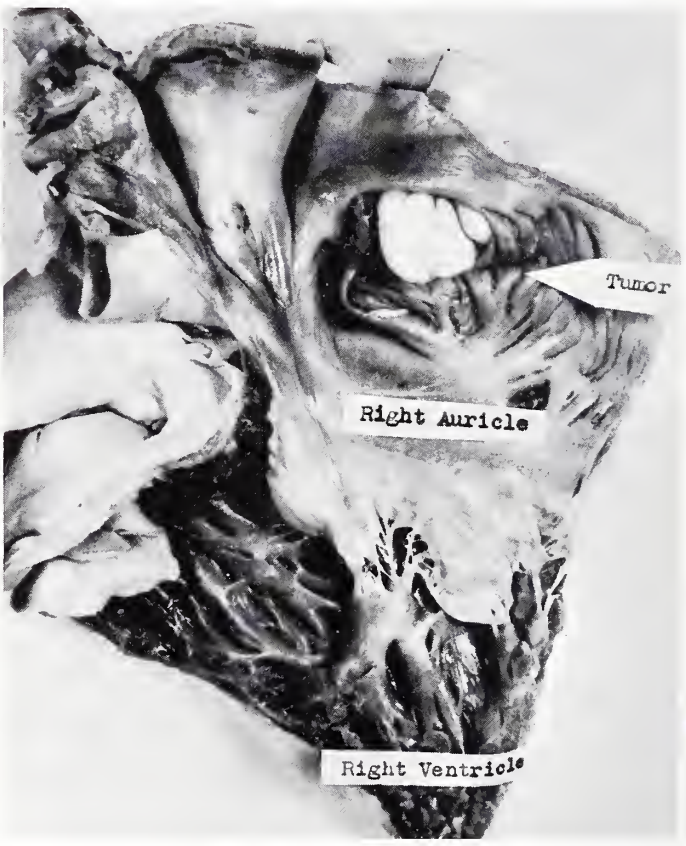

Figure 36
LIPOMA

Unlike lipomatous hypertrophy, lipomas elsewhere in the heart are encapsulated, white or yellow-white, and similar to lipomas elsewhere in the body. So-called true lipomas are found in the ventricular myocardium, atrial myocardium, as shown here, and pericardium.

trapped in the tumor and were originally diagnosed as rhabdomyomas. In our experience, the cardiac rhabdomyoma is primarily a tumor of childhood, and rarely occurs in anyone over 20 years of age. Like the cardiac fibroma in which cardiac myofibers may be entrapped, "spider cells" were not identified in any lipoma. The association of cardiac lipoma and tuberous sclerosis has been reported. Lipomas may be present both in the heart and viscera of patients with tuberous sclerosis in the absence of cardiac rhabdomyomas.

Treatment. Lipomas located in the pericardium or arising from the epicardial surface of the heart are effectively treated

TABLE 11

LIPOMAS OF THE HEART AND PERICARDIUM
CLINICOPATHOLOGIC CORRELATIONS IN 13 PATIENTS

Patient	Age	Sex	Site	Cardiac Symptoms	Duration	Pathology
LIPOMAS OF THE HEART (EXCLUDING LIPOMATOUS HYPERTROPHY OF THE ATRIAL SEPTUM)						
1	24 yrs	F	Ventricular septum, left ventricle	None		Tuberous sclerosis
2	25 yrs	F	Left ventricle, multiple	None		Tuberous sclerosis
3	25 yrs	F	Right and left ventricles	None		Tuberous sclerosis
4	39 yrs	F	Epicardial, right ventricle	Cardiomegaly/pericardial effusion	2 yrs	Surgical excision of lipoma
5	44 yrs	M	Epicardium, left ventricle	Cardiomegaly/precordial pain	1 yr	Surgical excision of lipoma
6	44 yrs	M	Atrial appendage, right	Angina/old myocardial infarct	4 yrs	Sudden death
7	47 yrs	M	Atrial appendage, left	None		Astrocytoma
8	67 yrs	M	Right atrium	None		Berry aneurysm
LIPOMAS OF THE PERICARDIUM						
9	40 yrs	M	Pericardium, right costophrenic angle			Surgical excision of lipoma
10	47 yrs	M	Pericardium, right costophrenic angle	Precordial pain	months	Surgical excision of lipoma
11	52 yrs	M	Pericardium, right costophrenic angle			Myocardial infarct, acute
12	57 yrs	M	Pericardium, left costophrenic angle	Precordial pain	months	Surgical excision of lipoma
13	66 yrs	M	Pericardium, base of aorta, intrapericardial	Atrial and ventricular premature contractions	1 yr	Cerebrovascular accident, myocardial infarct, old, healed

by surgical excision. The majority of these tumors, however, appear to be asymptomatic and no treatment is indicated.

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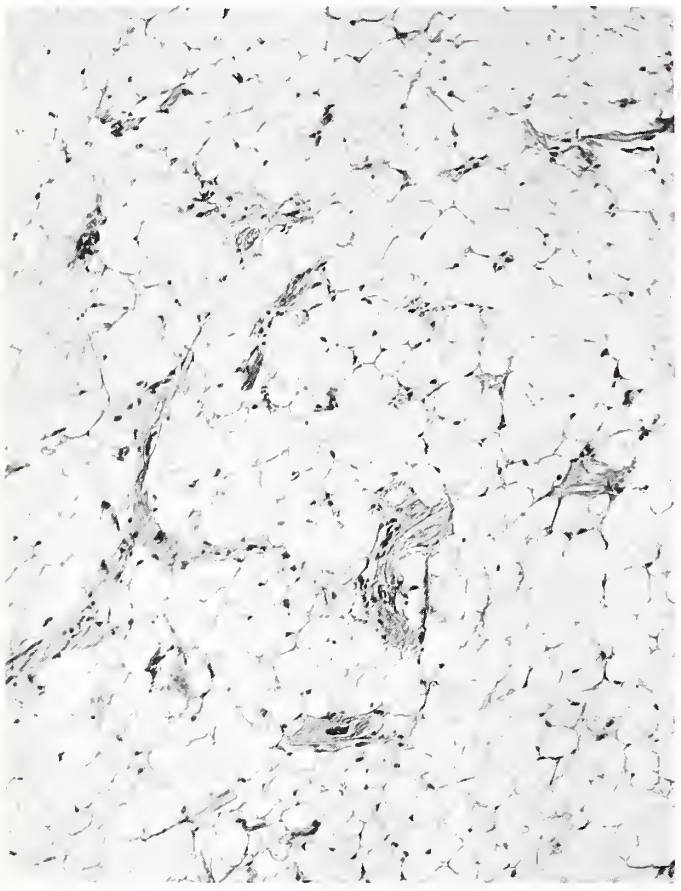


Figure 37
LIPOMA

True lipomas are composed virtually entirely of mature adipose tissue. Fetal fat is rarely, if ever, identified. As with lipomas elsewhere in the body, cardiac lipomas contain varying amounts of fibrous tissue, often arranged in broad septae. Blood vessels, especially capillaries, are occasionally abundant. X80.

HEMANGIOMA

SYNONYMS AND RELATED TERMS: Capillary hemangioma; cavernous hemangioma; intramuscular hemangioma; hemangioendothelioma.

Definition. Hemangiomas are all comprised of benign proliferations of endothelial cells, usually forming channels containing blood. The synonyms are merely descriptions of the varying growth patterns and do not necessarily imply differences in prognosis. Histologically, hemangiomas arising in the heart are identical to hemangiomas elsewhere in the body, although they are remarkably rare in the heart.

Clinical Aspects. Hemangiomas may occur at any site in the heart, and, in our series, tumors were found in both ventricles, in the right atrium, on the epicardial surface of the heart, and in the pericardium (Table 12). Hemangiomas of the left atrium have also been reported. In more than half the patients, who ranged in age from seven months to 80 years, these tumors were incidental findings at necropsy. Symptoms in the remaining patients were dependent on the location of the tumor. In three patients (1, 4, 6), the tumors were intracavitary and mimicked the symptoms of patients with myxomas. Two patients (5, 9) had a mass discovered on routine chest x-ray and were operated on with the probable diagnosis of pericardial cyst. A hemangioma was found in both patients. The final two patients presented with cardiomegaly and recurrent pericardial effusions. The cardiac enlargement was suggestive of a mass lesion, and, at operation, an intramyocardial hemangioma was discovered in both patients.

Description. Characteristically, hemangiomas appear red and hemorrhagic (pl.

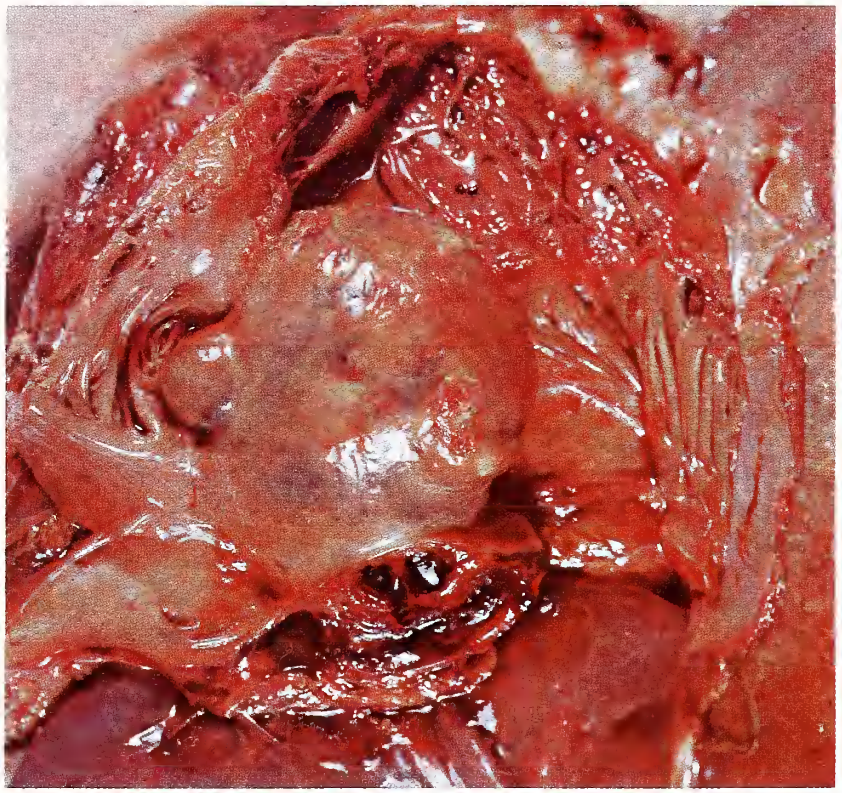
TABLE 12

CARDIAC HEMANGIOMA
CLINICOPATHOLOGIC CORRELATIONS IN 15 PATIENTS

Patient	Age	Sex	Site	Cardiac Symptoms	Comment
1	7 mos	M	Right atrium, intracavitary	Congestive heart failure	Surgical excision; alive and well one year later
2	8½ yrs	F	Left ventricle, apex, intramyocardial	Cardiomegaly, pericardial effusion	Surgical excision; alive and well two years later
3	12 yrs	F	Left ventricle, anterior, intramyocardial	Cardiomegaly, pericardial effusion, congestive heart failure	Surgical biopsy; x-ray therapy; no follow-up
4	14 yrs	F	Left ventricle, intracavitary	Systolic ejection murmur, congestive heart failure	Diagnosed as acute rheumatic heart disease; no valvular disease at necropsy
5	22 yrs	M	Pericardium, left costophrenic angle	Mass on x-ray	Surgical excision; alive and well
6	24 yrs	M	Right atrium, intracavitary	Syncope, congestive heart failure for seven years	Surgical excision unsuccessful (intraoperative death)
7	26 yrs	M	Epicardium, right ventricle	None	Incidental finding
8	39 yrs	M	Right ventricle outflow tract		Incidental finding
9	56 yrs	M	Epicardium, left/right ventricle, intrapericardial	Mass by x-ray	Surgical excision; alive and well
10	61 yrs	M	Ventricular septum	None	Incidental finding
11	68 yrs	M	Mitral valve, posterior leaflet, ventricular aspect at base	None	Incidental finding
12	68 yrs	M	Ventricular septum, intracavitary left ventricle	None	Incidental finding
13	71 yrs	M	Epicardium, left ventricle		Incidental finding
14	79 yrs	M	Right atrium, intracavitary		Incidental finding
15	80 yrs	M	Epicardium, right ventricle	Mass by x-ray	Incidental finding

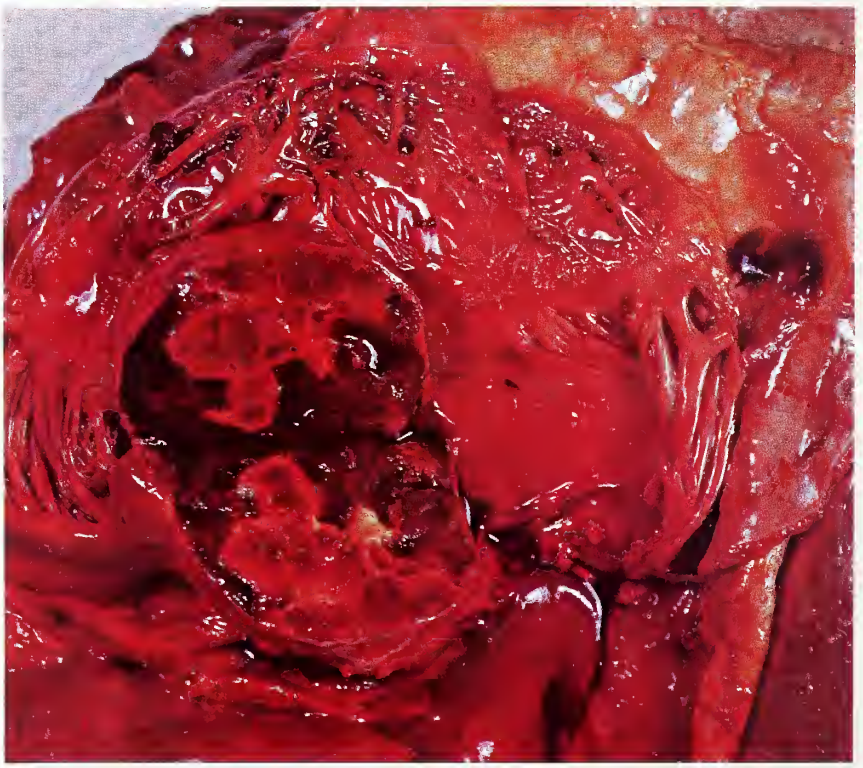
IV-A, B). Microscopically, they are classified according to the morphologic pattern and interrelationship of the vascular channels, endothelial cells, and supporting stroma. Capillary hemangiomas consist of haphazardly arranged, often closely packed capillary structures, lined by flattened endothelial cells with minimal intervening stroma (figs. 38, 39). Cavernous hemangiomas consist of widely dilated vascular channels lined by flattened endothelial cells, with focal abundant connective tissue between the larger vascular channels (fig. 40). Hemangioendotheliomas resemble capillary hemangiomas; however, the vascular spaces are lined by rounded, often

PLATE IV
HEMANGIOMA*



A

A. This hemangioma fills the right atrium. Occasionally, hemangiomas are intracavitary and should be considered in the differential diagnosis of intracavitary mass lesions.



B

B. When transected, the vascular nature of the hemangioma is usually readily apparent.

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*Courtesy of Dr. Giorgio Baroldi, Milan, Italy; from Baroldi, G., Colombo, F., and Manion, W. C. Benign primary hemangioma of the right atrium of the heart. Report of a case. Med. Ann. D. C. 36:287-290, 1967.

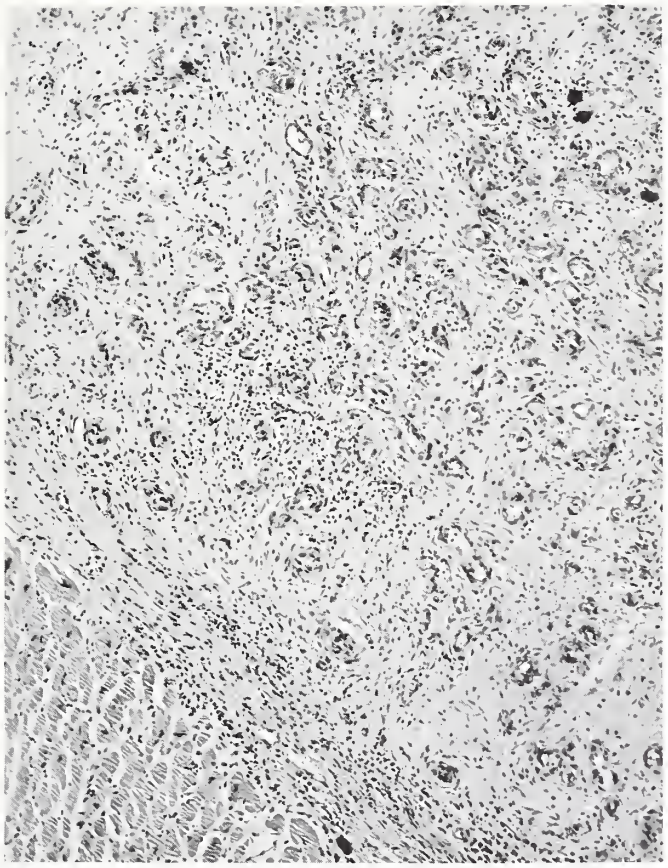

Figure 38
HEMANGIOMA

The capillary hemangioma is composed of small vascular channels lined by conspicuous endothelial cells. This tumor may consist of a solid mass of capillary channels with little intervening stroma, or the fibrous stroma may be abundant, as shown here, and separate the vascular channels into small clusters. Lymphocytes and plasma cells are often prominent, especially in intracavitary hemangiomas and in tumors situated just beneath the endocardium. X75.

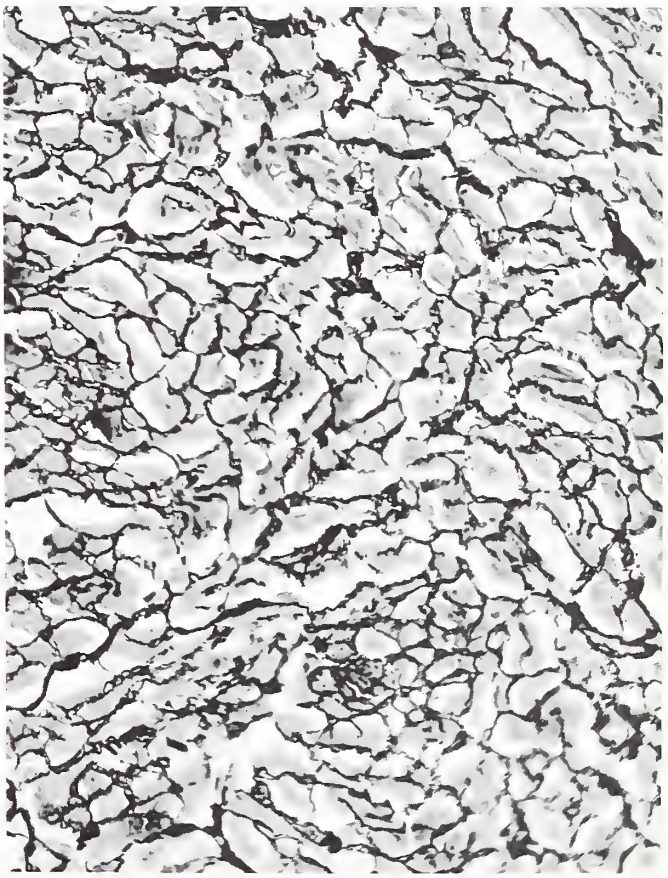

Figure 39
HEMANGIOMA

The vascular nature of the solid capillary hemangioma is best appreciated with the reticulum stain. The reticulum stain outlines the capillary sheath and clearly demonstrates the proliferation of cells within the capillary lumen. Laidlaw reticulum stain, X165.

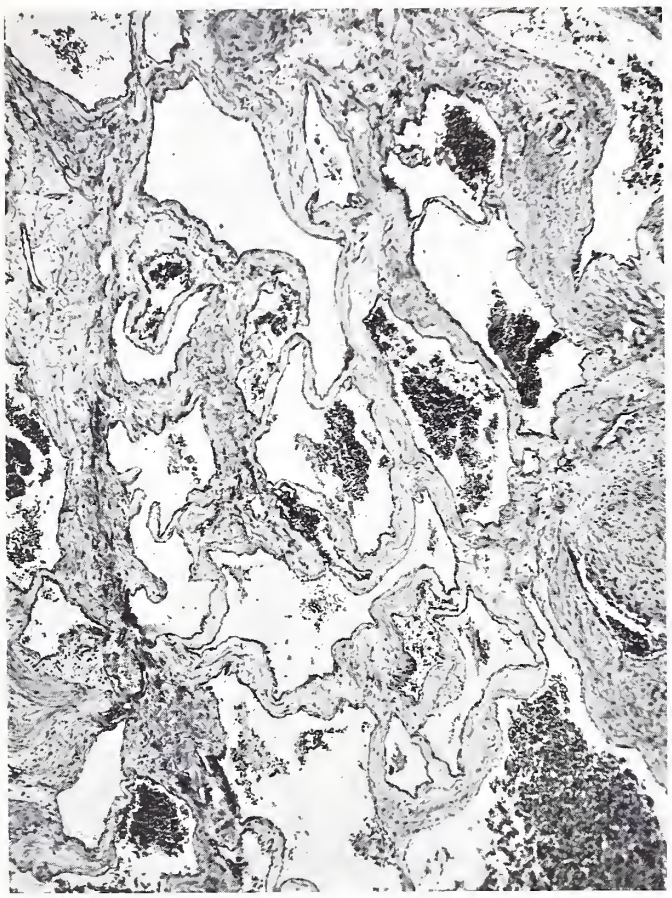

Figure 40
HEMANGIOMA

The cavernous hemangioma is composed of large dilated vascular channels lined by flattened inconspicuous endothelial cells. The vascular channels are usually filled with erythrocytes, and the intervening fibrous stroma is prominent. X45.

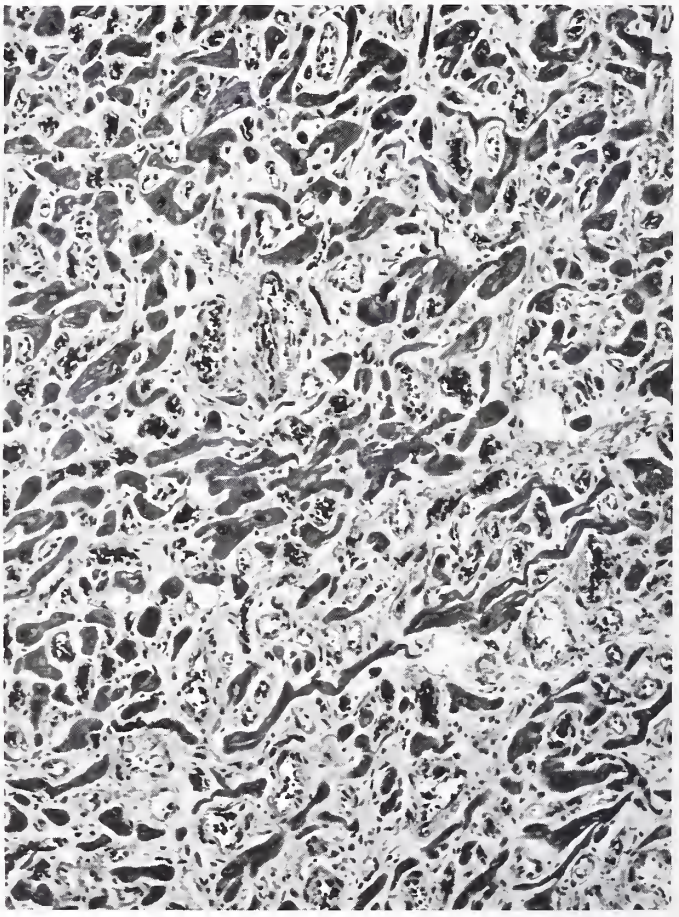

Figure 41
HEMANGIOMA

The intramuscular hemangioma is a diffuse angiomatosis. These tumors are poorly circumscribed and the capillary channels appear to proliferate between myofibers, distorting the normal architecture of the myocardium. The intramuscular hemangioma, in spite of its diffuse growth pattern, is benign and should not be mistaken for an angiosarcoma. X110.

multilayered, endothelial cells which occasionally appear to fill the entire vascular channel. Reticulum stains clearly define the vascular nature of the hemangioendothelioma (fig. 39). Intramuscular hemangiomas consist of clusters of vascular channels, usually capillaries, insinuated between muscle bundles in the myocardium (fig. 41). The muscle bundles are compressed and distorted, but not replaced by the insinuating vascular channels. We have never seen a benign hemangiopericytoma, a fourth type of hemangioma, in the heart. However, there is no reason to assume that this vascular tumor, which consists of proliferating pericytes on the extraluminal side of the capillary basement membrane, cannot occur in the heart.

Treatment. When these tumors produce symptoms, the treatment of choice is surgical excision. The varied presentation of the hemangiomas points out the importance of a complete clinical evaluation in all patients with cardiac symptoms.

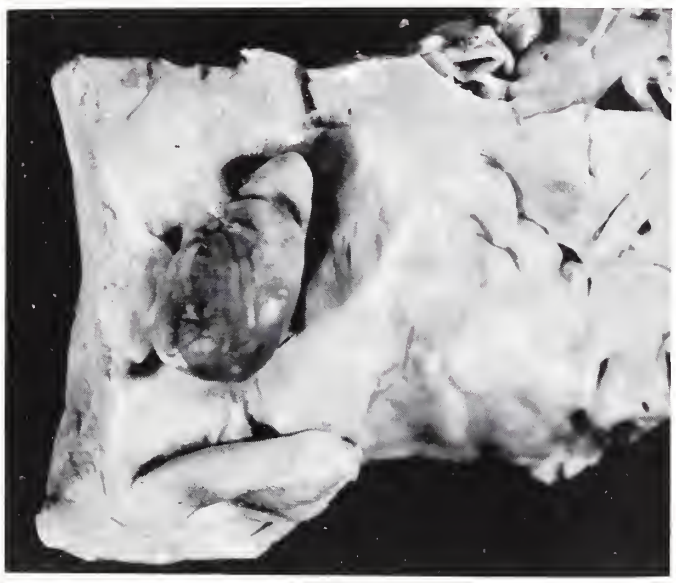

Figure 42
VARIX

The varix is a dilated, thrombosed venous channel. In the heart, it most commonly occurs in the subendocardium of the atrial and ventricular septum and is occasionally pedunculated—hence, the term "hemorrhoids of the heart."

Varix

Definition. Varices are dilated blood vessels in the subendocardium which are frequently mistaken for hemangiomas (fig. 42). They may occur anyplace in the heart, but are most common in the subendocardium of either atrium or ventricle.

Description. Varices are easily distinguished microscopically from hemangiomas (fig. 43). The varix consists of a single or cluster of normally formed vascular channels, usually veins, which are dilated and frequently thrombosed, morphologically

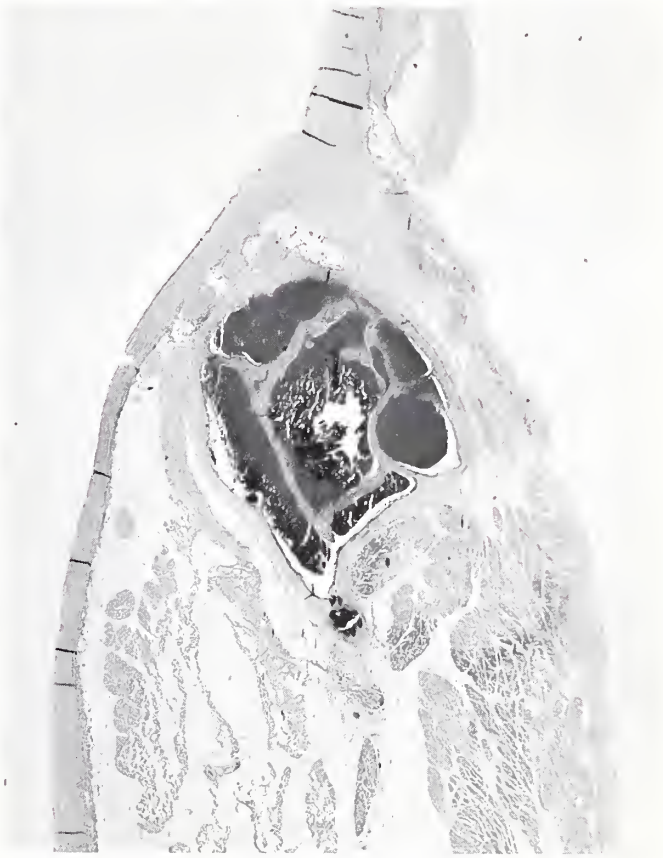

Figure 43
VARIX

The varix consists of single or clusters of thin-walled, dilated, and thrombosed vascular channels. Although most common in the subendocardium, they are occasionally found in the myocardium. This varix, an incidental finding at autopsy, was located in the atrial septum. X9.

resembling hemorrhoids. The exact incidence of varices is unknown; however, they are usually incidental findings.

Blood Cyst

Definition. A blood cyst is a separation or cleft between endocardial cells or between the supporting stroma and endocardial cells, creating a channel containing blood, probably derived from the cavitary blood of the heart. These cysts are not true vessels or hemangiomas and have no apparent clinical significance.

Description. Blood cysts are found on the endocardium, particularly the valvular endocardium, in newborns and infants (fig. 44). The cysts are usually lined by normal endocardial cells, and the lining cells are not delimited from surrounding endocardial cells by a basement membrane. Occasionally, the intravalvular portion of the blood cyst is not lined by endocardial cells, but consists of the endocardial stroma.

Figure 44
BLOOD CYST

Blood cysts, common in newborns and infants, are found most frequently on the mitral and tricuspid valves. A small blood cyst of the tricuspid valve (arrow) is illustrated here. The blood cyst is not a hemangioma but rather a blood-filled cleft between normal endocardial cells. These cysts have no apparent clinical significance and are thought to regress spontaneously.

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MESOTHELIOMA OF THE ATRIOVENTRICULAR NODE

SYNONYMS AND RELATED TERMS: Conduction tumor; lymphangioendothelioma; coelotheliome Tawarien; endodermal inclusion tumor.

Definition. Conduction tumors are always located in the region of the atrioventricular node. They are composed of nests of mesothelial cells and are, therefore, mesotheliomas of the atrioventricular node. We believe they arise from mesothelial rests similar to adenomatoid tumors of the ovary and testis, and are always benign. To distinguish these tumors from mesotheliomas of the pericardial surface, we prefer the designation conduction tumor, but will use the more descriptive term—mesothelioma of the atrioventricular (A-V) node.

Clinical Aspects. As has been well documented, the majority of these patients have partial or complete atrioventricular heart block, usually of long duration, and often die either of complete heart block or ventricular fibrillation. This tumor has been referred to as the smallest tumor which

TABLE 13

MESOTHELIOMA OF THE ATRIOVENTRICULAR NODE CLINICOPATHOLOGIC CORRELATIONS IN 12 PATIENTS

Patient	Age	Sex	Duration of Symptoms	Symptoms	Cause of Death
1	11 mos	M	8 mos	2 and 3° A-V block Wenckebach phenomenon	Hydrocephalus
2	8 yrs	F	10 days	Fever, nausea	Sudden unexpected death
3	8 yrs	M	4 yrs	2 °A-V block, syncope	Stokes-Adams syndrome
4	23 yrs	F		? History of rheumatic heart disease as a child but without symptoms	Sudden unexpected death
5	23 yrs	F	5 mos	1° and 2 °A-V block	Acute cholecystitis, sepsis
6	29 yrs	F	15 yrs	Dyspnea, bradycardia	Congestive heart failure
7	48 yrs	F	4.5 yrs	Complete heart block, (treated with transvenous pacemakers for 4 years)	Sudden unexpected death
8	49 yrs	F	37 yrs	Bradycardia, syncope, Stokes-Adams syndrome, complete A-V block	Sudden death associated with severe chest pain
9	53 yrs	F	35 yrs	Syncope, complete A-V block murmur of aortic stenosis (confirmed at autopsy)	Ventricular fibrillation
10	62 yrs	M	4 yrs	Palpitations, angina, complete A-V block (treated with transvenous pacemaker)	Ventricular fibrillation
11	69 yrs	M	6 mos	Paroxysmal atrial tachy-cardia, 1 ° A-V block	Ventricular fibrillation
12	71 yrs	F	12 yrs	Bradycardia, complete A-V block	Congestive heart failure

causes sudden death. To reemphasize these points, the cardiac findings in 12 patients in the AFIP collection have been summarized in Table 13. Many of the patients were thought to have chronic rheumatic heart disease, either by history or on the basis of the rhythm disturbances; however, only one patient (9) actually had valvular heart disease confirmed at necropsy. None of the patients had significant coronary artery disease with 75 percent or greater occlusion of a major coronary artery. Atri-

oventricular block of varying degree was the major finding in the majority of patients; clinically, the etiology of the conduction disturbance was unclear. The patients ranged in age from 11 months to 71 years, which is similar to that reported in the literature.

Description. Mesotheliomas of the A-V node are usually poorly circumscribed, slightly elevated nodules located in the atrial septum just above the septal leaflet of the tricuspid valve in the region of the atrioventricular node (fig. 45). They are usually multicystic (figs. 46, 47).

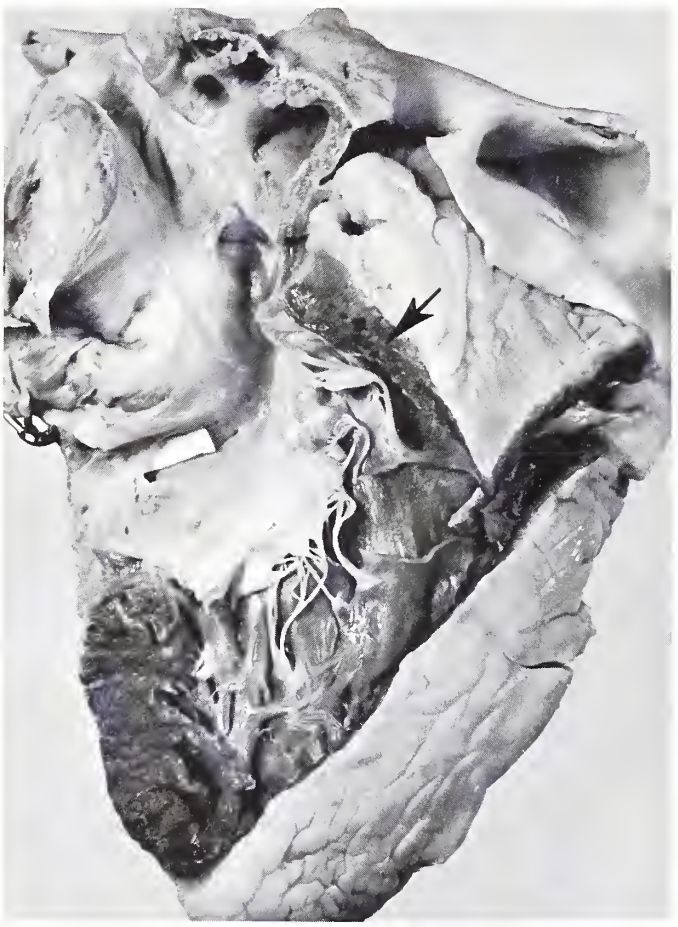

Figure 45
MESOTHELIOMA OF THE A-V NODE

Mesotheliomas of the atrioventricular node are located in the atrial septum at, or close to the region of the atrioventricular node. In this case, the transected atrial septum (arrow) is thickened and spongy. The atrioventricular node lies just above the junction of the septal and anterior leaflets of the tricuspid valve, to the immediate right of the marker in the coronary sinus. (From Manion, W. C., Nelson, W. P., Hall, R. J., and Brierty, R. E. Benign tumor of the heart causing complete heart block. Am. Heart J. 83:535-542, 1972.)

Microscopically, the cysts are lined by uniform polygonal cells, frequently multilayered, and with a suggestion of a "brush" border (fig. 48). Between the large cysts are multiple nests of cells of markedly varying size. The large nests often have a central lumen, whereas the small nests appear solid (figs. 49, 50). In many areas, especially in the smaller nests, the cells are often squamoid in appearance (fig. 51). Many of the nuclei are ovoid and have a cleftlike longitudinal indentation, resembling so-called "coffee-bean" nuclei. The periodic acid-Schiff reaction (PAS) and the alcian blue stain will demonstrate foci of positive staining. PAS positivity is variable, although usually the eosinophilic material within the cyst lumens and intercellular spaces is intensely positive, and scattered foci of intracellular positivity are also present. The intracellular positivity is partially abolished by prior diastase digestion, while the foci of intercellular PAS positivity are frequently unaffected by prior diastase digestion. All conduction tumors stain positively with alcian blue, although the staining reaction is frequently weak. The material within the central lumen and intercellular spaces, as well as intracellular material, stains positively, but intracellular positivity is more prominent, especially under high magnification. Both the intracellular and intercellular positive alcian blue reaction is abolished by prior hyaluronidase digestion. Rarely, foci of intercellular material are weakly positive with Best's mucicarmine.

The cellular nests and the cystic structures are set in a dense tissue stroma. Collagen and elastic fibers are abundant,

and mast cells are frequent. The tumor often replaces all, or part of the atrioventricular node and may extend upward into the atrial septum and downward into the atrioventricular bundle. We have never seen a mesothelioma of the A-V node that extended into the ventricular myocardium or into the tricuspid valve, nor have we seen a metastasis from a conduction tumor.

Ultrastructurally (fig. 52), mesotheliomas of the A-V node are strikingly similar to adenomatoid tumors of the ovary and testis. The cysts and cellular nests are composed of irregular-shaped polygonal cells. The polygonal cells lining the lumen have numerous widely spaced microvilli, and the cells are joined by tight junctions with desmosomes at the luminal surface. The cells are multilayered, and there are numerous intercellular spaces bound on all sides by tight junctions and desmosomes. Tight junctions and desmosomes are not present against the basal lamina that surrounds the cysts and cellular nests. Intracellular spaces, bounded by desmosomes and hemidesmosomes, are features of mesothelial cells and are further evidence that the conduction tumor is of mesothelial origin. These tumors probably derive from embryonic rests of mesothelial cells entrapped in the atrioventricular node region during embryonic development.

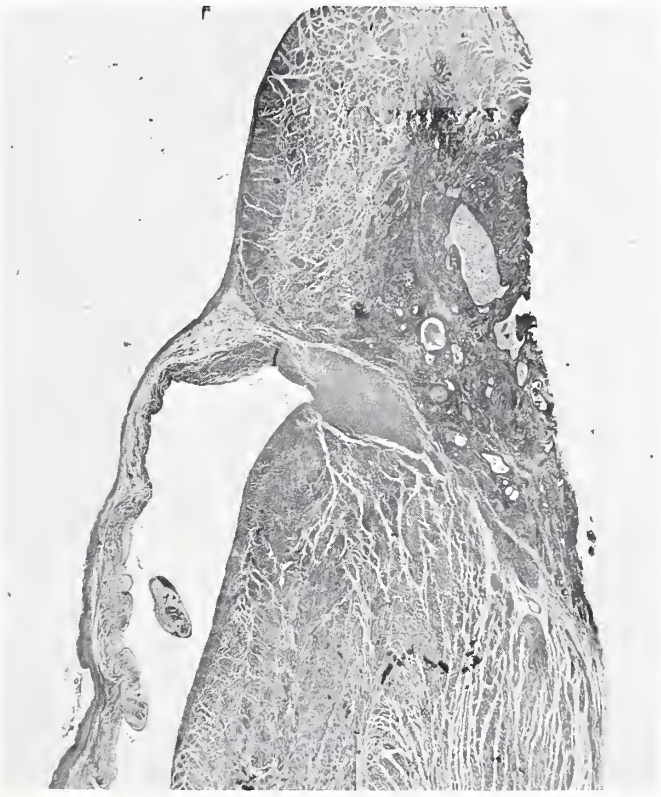

Figure 46
MESOTHELIOMA OF THE A-V NODE
The tumor is confined to the atrial septum, delineated from the ventricular myocardium by the fibrous annulus. The tumor is primarily subendocardial and only rarely replaces the full thickness of the atrial septum. This tumor completely replaced the atrioventricular node. X6.

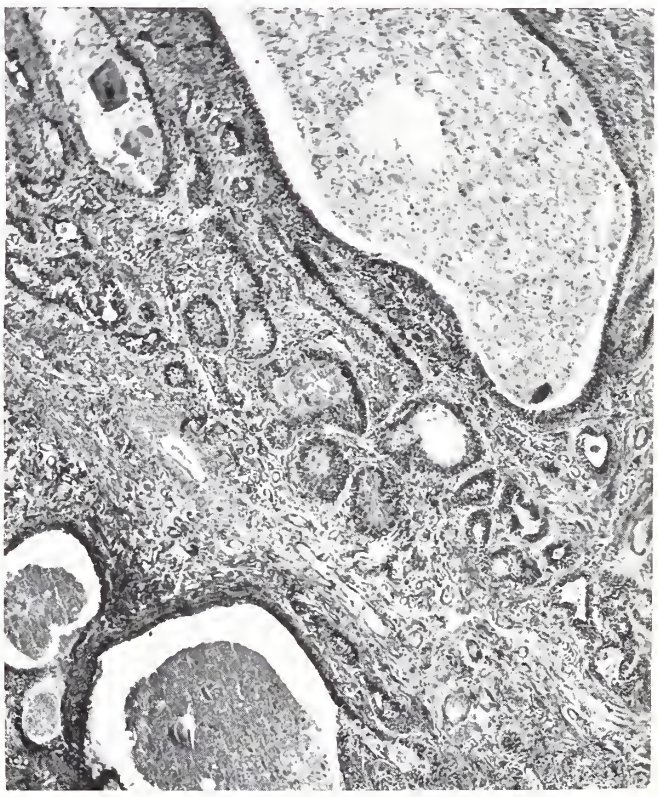

Figure 47
MESOTHELIOMA OF THE A-V NODE
The tumor consists of varying sized spaces and channels set in a dense fibrous tissue stroma. The amorphous material which fills the larger spaces stains positively with PAS, and this is usually unaffected by prior diastase digestion. X50.

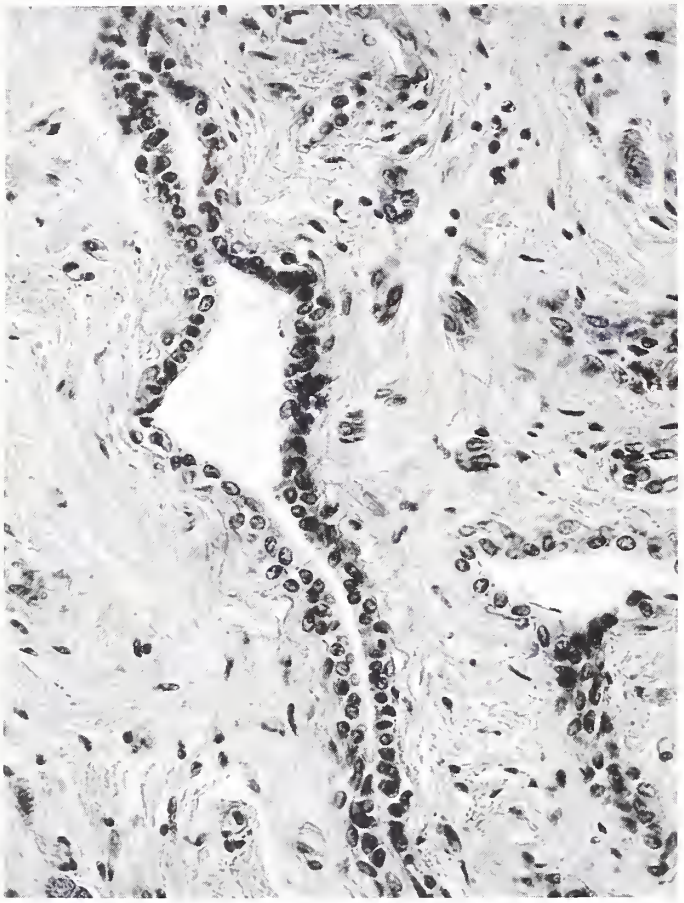

Figure 48
MESOTHELIOMA OF THE A-V NODE
(Figures 48 and 49 from same case)

The smallest channels in the tumors are usually lined by a flattened single layer of cells. These channels often contain a proteinaceous material which has led to the mistaken interpretation that these are lymphatic channels. The proteinaceous material, within these spaces and the lining cells, stains positively with alcian blue. This staining reaction is abolished by prior hyaluronidase treatment suggesting that the proteinaceous material is a mucopolysaccharide. X305.

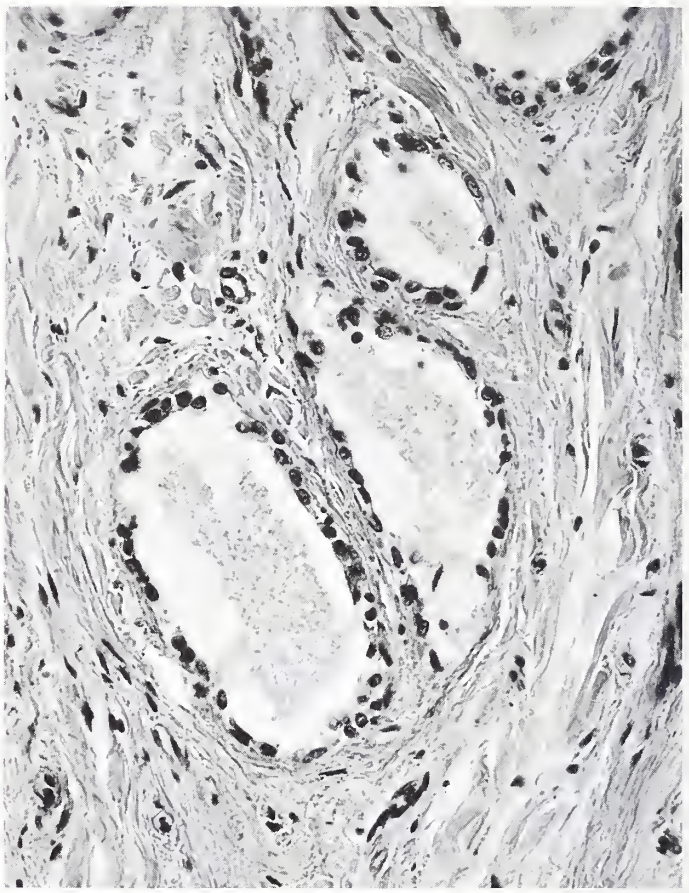

Figure 49
MESOTHELIOMA OF THE A-V NODE

Larger channels in the tumor, often in continuity with the smaller channels shown in figure 48, are lined by rounded cells. These cells are multilayered and the nuclei are ovoid and vesicular. These cells closely resemble normal mesothelial cells. X305.

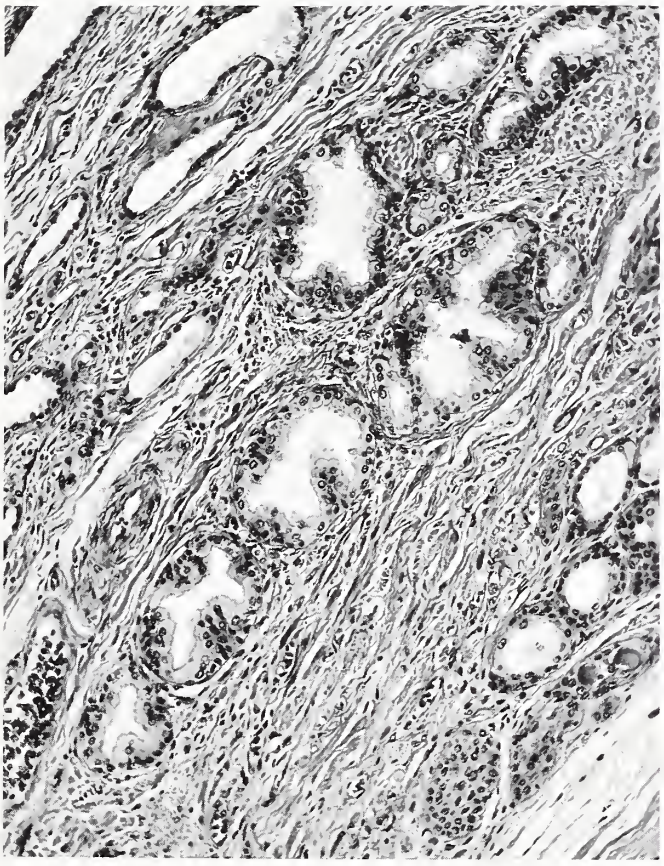

Figure 50
MESOTHELIOMA OF THE A-V NODE
(Figures 50 and 51 from same case)

The cells lining the smaller channels and spaces in the tumor vary widely in appearance. Occasionally, the lining cells are plump, cuboidal, or columnar and there is a suggestion of cilia or a brush border by light microscopy. X150.

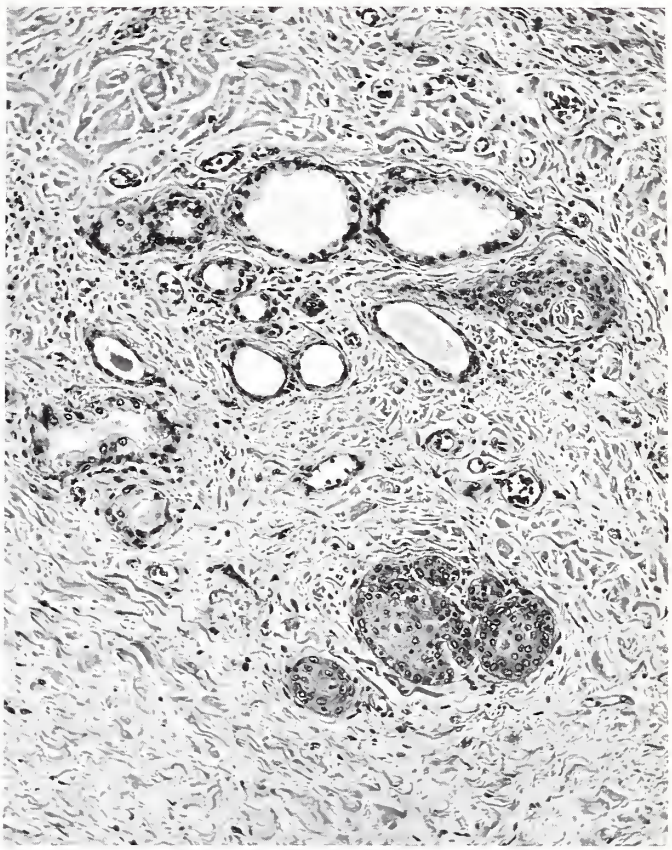

Figure 51
MESOTHELIOMA OF THE A-V NODE

In other areas in the same tumor shown in figure 50, small nests of cells which appear squamoid are present. In spite of the squamoid appearance of these cell nests, keratin and intercellular bridges cannot be demonstrated by light microscopy. X115.

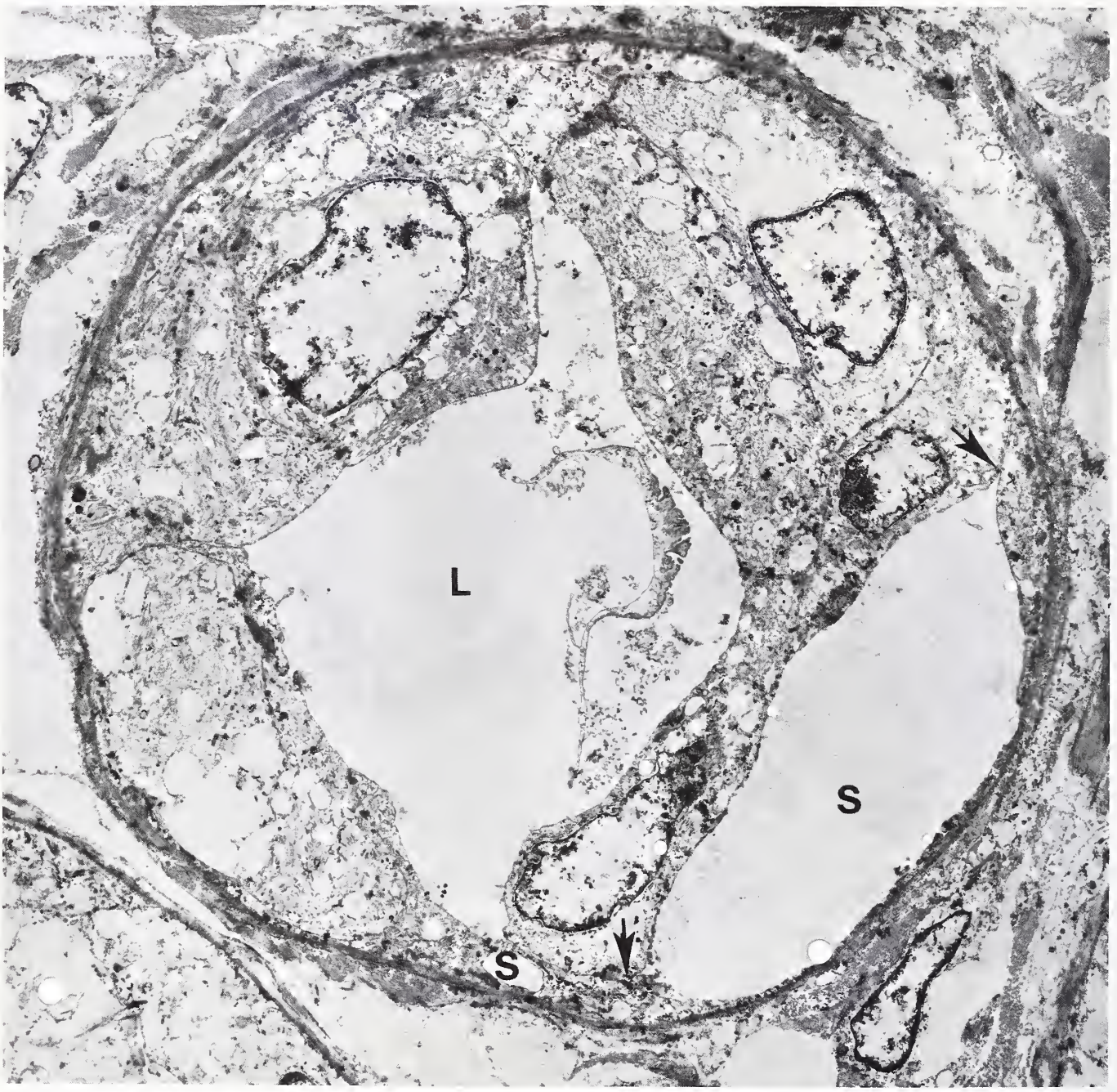

Figure 52
MESOTHELIOMA OF THE A-V NODE

Ultrastructurally, the many apparently different morphologic cell types which line the spaces and channels of the tumor are identical. The cells are polygonal, with large ovoid nuclei. Intercellular spaces (S), separate from the lumen (L), are prominent and bounded by specialized junctions usually of the desmosome type (arrows). Ultrastructurally, the cells of the tumor are similar to mesothelial cells. Uranyl acetate and lead citrate, X5775.

Treatment. Since both complete and partial atrioventricular block is the major clinical expression of this tumor, the use of a pacemaker to maintain normal ventricular function appears indicated. However, even with cardiac pacing, two patients in our series developed ventricular fibrillation. Cardiac pacing, coupled with drug therapy to suppress residual atrioventricular nodal activity and possible accessory atrioventricular pathways, is probably indicated for these patients.

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TERATOMA

SYNONYMS AND RELATED TERMS: Intrapericardial teratoma; pericardial teratoma; intrapericardial bronchogenic cyst; intrapericardial dermoid cyst.

Definition. A teratoma, by definition, must contain elements derived from all three germ layers. The majority of the tumors fulfilling these criteria are extracardiac but intrapericardial, and arise from the base of the heart, usually attached to the root of the pulmonary artery and aorta. Although intracardiac teratomas have been reported, the majority of the reports describe cysts that do not include all three germ layers (see bronchogenic cyst and mesothelioma of the A-V node).

Clinical Aspects. There are 14 intrapericardial teratomas in the AFIP collection. The patients ranged in age from less than one day to 42 years; however, 11 were in the pediatric age group. Interestingly, all were female, with one exception—a 10 week old infant boy.

Two patients in this series died suddenly and unexpectedly; the remaining 12 patients all presented with signs and symptoms relating to the heart. Dyspnea and cardiomegaly were among the presenting symptoms in each patient. In addition, the infants were usually cyanotic and, occasionally, had cardiac murmurs. With the aid of newer diagnostic technics in cardiology, a diagnosis of an extracardiac mass was established in each of the more recent cases (post 1960) in this series. The teratoma was excised from eight patients; six were alive and well without evidence of recurrence at least two years following surgery, and two died during the postoperative period.

Description. Intrapericardial teratomas may assume massive proportions, measuring up to 15 cm. in greatest dimension. They are pear-shaped, usually smooth-surfaced and lobulated (fig. 53). On cut section, the teratoma contains numerous multiloculated cysts and intervening solid areas (fig. 54).

Microscopically, intrapericardial teratomas resemble teratomas elsewhere in the body, especially benign cystic teratomas of the ovary. The cysts are lined by ciliated columnar epithelium, stratified squamous epithelium, or pseudostratified mucin-secreting columnar epithelium (figs. 55, 56). Within the solid areas, foci of neural tissue are frequent, and collections of acinar structures replicating thyroid or pancreas are common (fig. 57). Collections

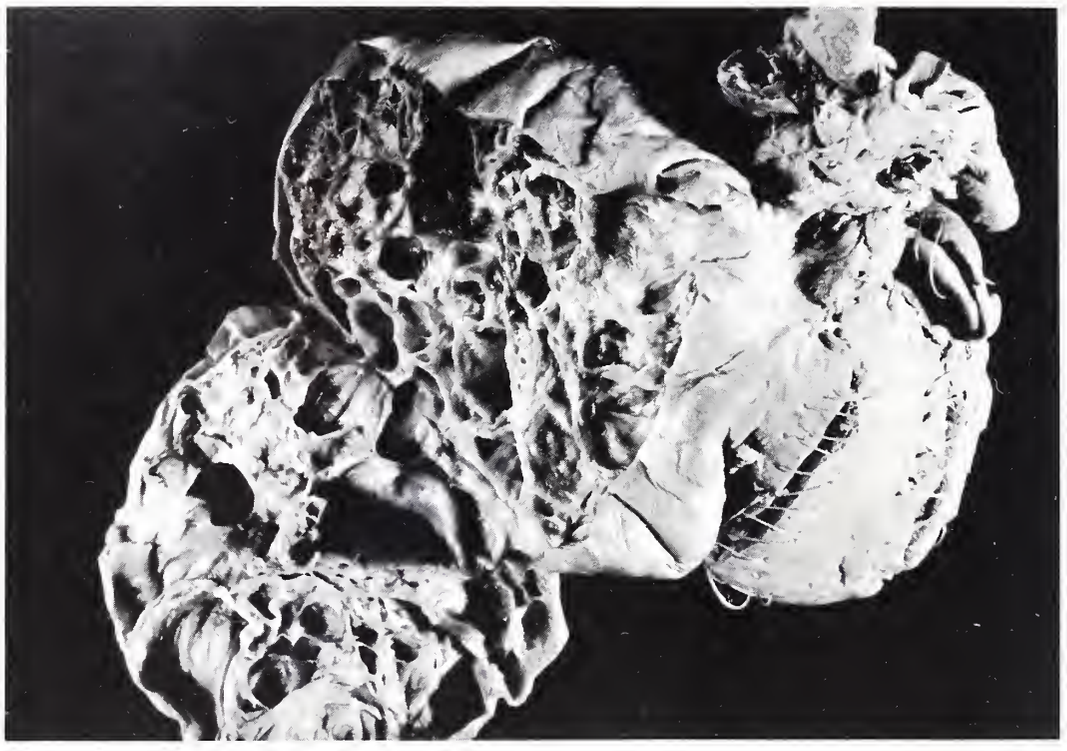

Figure 53
TERATOMA

Cardiac teratomas are usually intrapericardial tumors attached to the root of the pulmonary artery and aorta. The tumor may reach massive proportions and the transected surface is always multicystic.

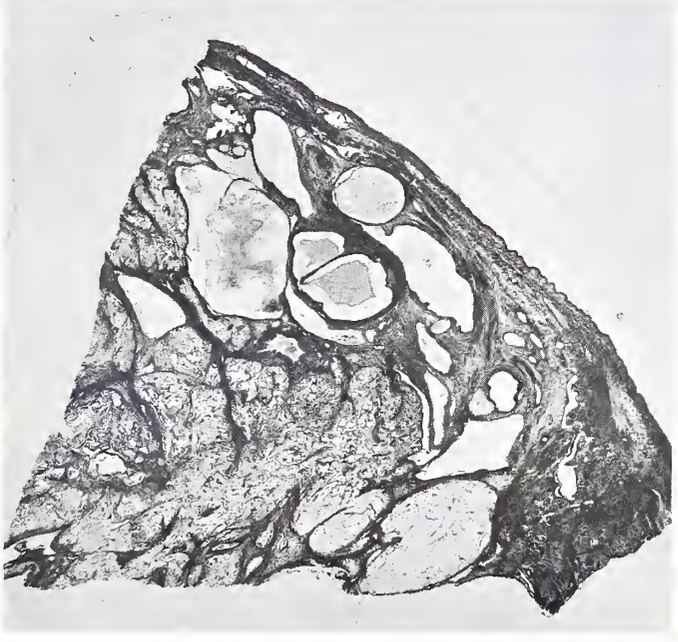

Figure 54
TERATOMA

The multicystic nature of the tumor with intervening solid areas is readily apparent. X3.

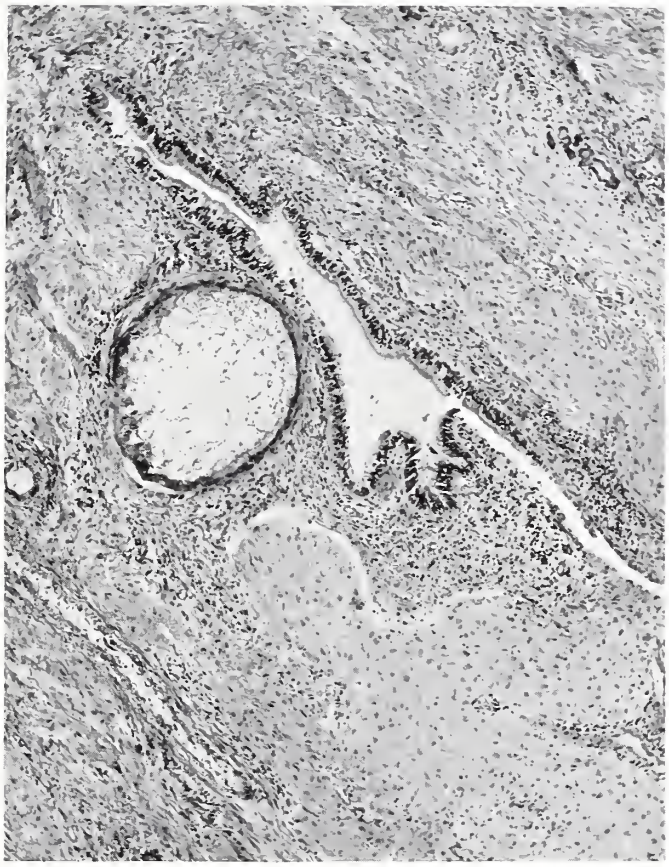

Figure 55
TERATOMA

The cystic spaces are lined by columnar cells with a ciliated border (respiratory epithelium), squamous cells, mucin producing epithelial cells, and flattened cells. The solid areas of the teratoma contain cartilage and bone, islands of smooth and striated muscle, neural tissue, and glandular structures which appear to replicate pancreas or thyroid. X50.

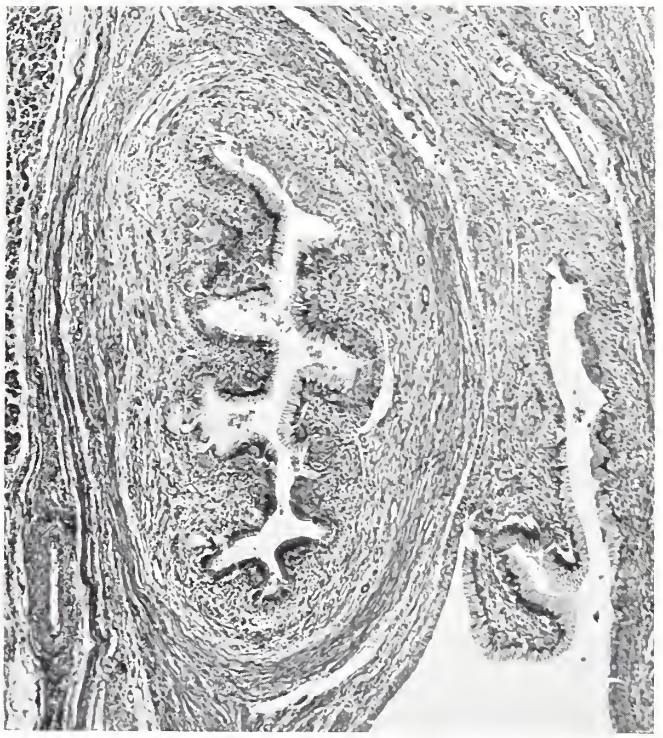

Figure 56
TERATOMA
(Figures 56 and 57 from same case)

Occasionally, portions of organs such as gut or bronchi are replicated in the teratoma, and many teratomas contain hair and teeth. X50.

of smooth muscle cells and striated muscle are haphazardly arranged within the stroma, replicating portions of skeletal muscle and bowel wall. Cartilage and bone, complete with hematopoietic tissue, are occasionally present. Derivatives of all three germ layers (endoderm, mesoderm, ectoderm) are reproduced in the teratoma.

Like all teratomas, intrapericardial teratomas have a malignant potential, although this is decidedly unusual. Nevertheless, all teratomas should be adequately sampled and sectioned to avoid overlooking the rare malignant examples.

Treatment. Surgical excision following diagnosis is the only effective therapy. These tumors are attached to the base of the heart at the root of the pulmonary artery and aorta, and usually receive their blood supply from vasa vasorum of these vessels. Effective removal must, therefore, include a careful dissection of the root of the great vessels.

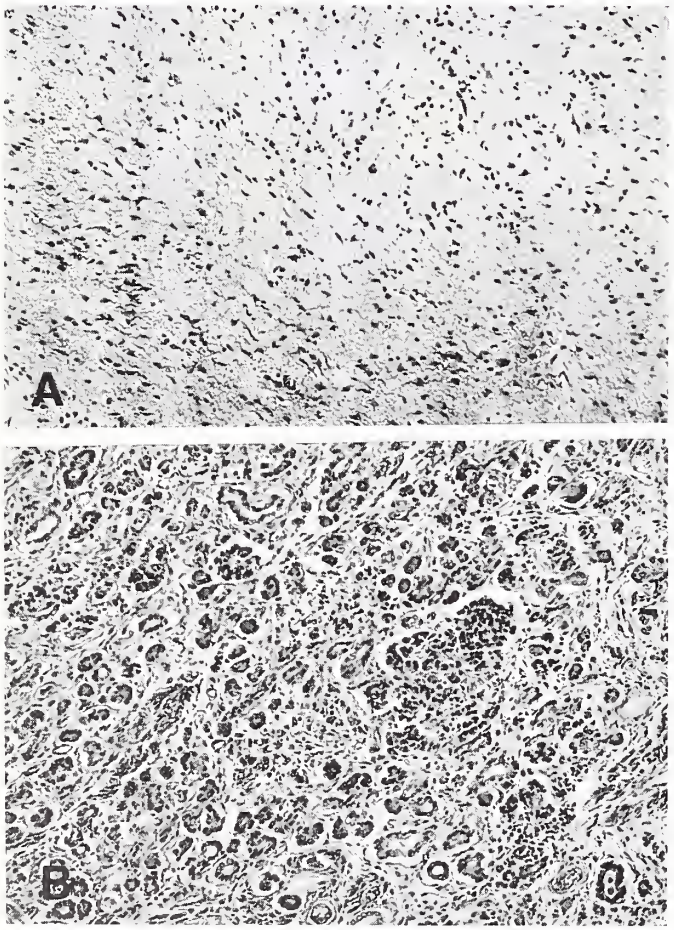

Figure 57
TERATOMA
(Figures 56 and 57 from same case)
Neural tissue (A) and pancreatic tissue (B) are frequently encountered in the teratoma. The teratoma must have components derived from all three germ layers. A and B X85.

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BRONCHOGENIC CYST

SYNONYMS AND RELATED TERMS: Inclusion cyst; epithelial cyst; heterotopic cyst; gastroenterogenous cyst.

Definition. Unlike teratoma, the bronchogenic cyst contains elements derived from only two germ layers—mesoderm and endoderm. The mesodermal elements are orderly, arranged around the endoderm-lined cyst, simulating a bronchus—hence, the term bronchogenic cyst. As in the skin and mediastinum, these cysts probably arise during embryologic development, either as a result of the migration of sequestered cells from the respiratory tree or the displacement of preformed cysts from their origin in the respiratory tract.

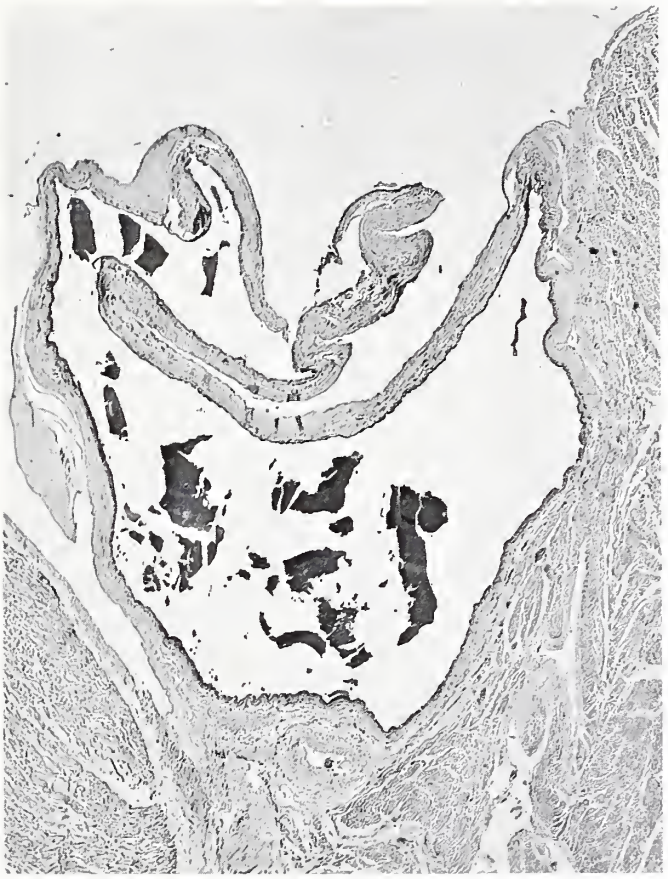

Figure 58
BRONCHOGENIC CYST
Bronchogenic cysts are misplaced elements of the respiratory tract, and, unlike teratomas, contain only elements derived from mesoderm and ectoderm. These cysts may be found in the heart or pericardium and usually resemble a bronchus. This cyst was located in the posterior papillary muscle of the left ventricle. X15.

Clinical Aspects. There are seven cysts of this type in the AFIP collection. Five patients were male and two were female—a sex distribution similar to that of bronchogenic cysts in the skin and subcutaneous tissues. In 6 of the 7 patients, the cyst was an incidental finding at necropsy. These six patients ranged in age from 36 to 75 years. The other patient, a 6 month old infant, presented with cardiomegaly and a loud systolic murmur. At necropsy, a large cyst protruded from the ventricular septum into the right ventricle, displacing the tricuspid valve into the right atrium.

Description. Bronchogenic cysts usually are submerged in the myocardium, although occasionally they may project into a cardiac chamber or into the pericardial cavity (fig. 58). These cysts rarely exceed 1 to 2 cm. in diameter. In the AFIP series, three cysts were located in the left ventricle (two in the posterior papillary muscle), two in the right ventricle, one in the atrioventricular sulcus, and one in the posterior interatrial groove.

Microscopically, the cysts are lined by ciliated columnar epithelium or cuboidal epithelium (fig. 59). Goblet cells are frequently present, and stratified squamous epithelium focally replaces the lining epithelium of many of the cysts, especially if

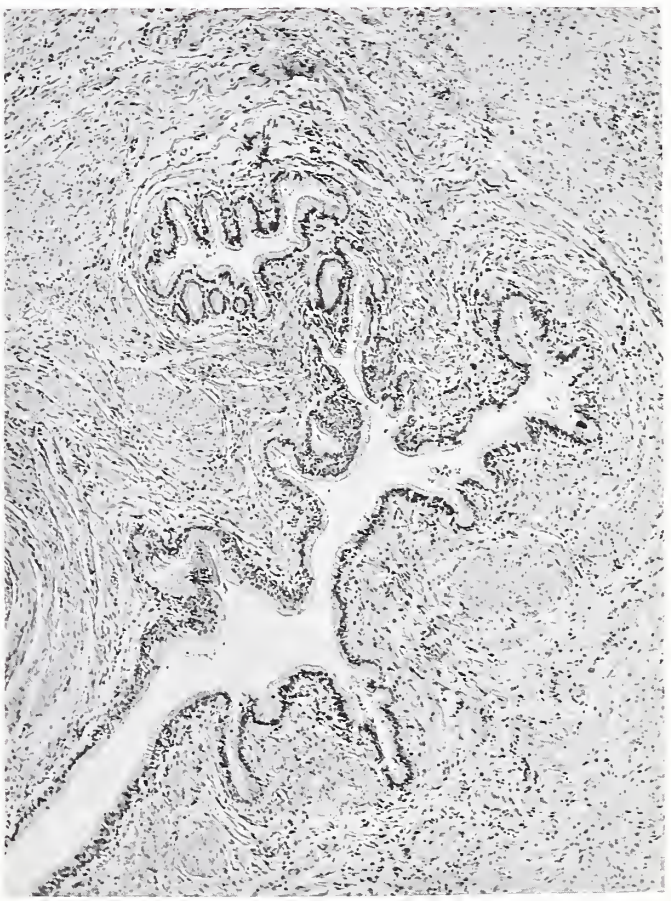

Figure 59
BRONCHOGENIC CYST
The cyst is usually lined by ciliated columnar epithelial cells and set in a dense fibrous tissue stroma. X60.

the cyst is inflamed (fig. 60). The wall of the cyst contains variable amounts of smooth muscle and cartilage as well as dense fibrous tissue. Lymphoid nodules and clusters of seromucinous glands are often present in the cyst wall. A teratoid origin of the bronchogenic cyst is excluded by complete absence of tissues other than those that can be explained on the basis of a malformation of the respiratory tract.

Treatment. These cysts are, with rare exception, incidental findings of no clinical significance. In the rare exception, surgical excision would be indicated for relief of symptoms.

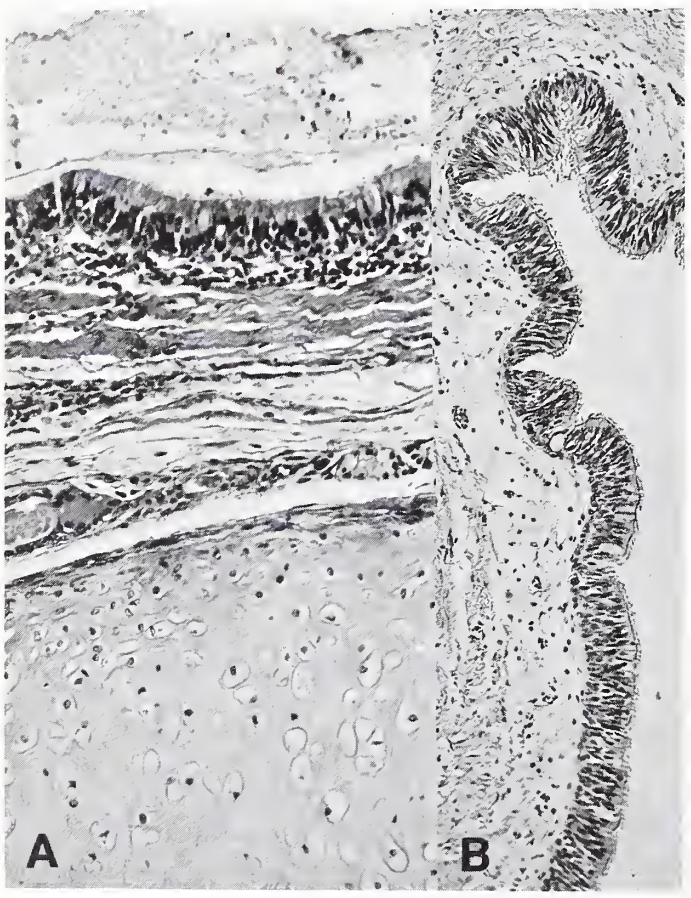

Figure 60
BRONCHOGENIC CYST

Islands of cartilage are frequently present beneath the epithelium (A) and seromucinous glands are occasionally present. At high magnification, cilia on the surface of the columnar cells are readily apparent, and scattered goblet cells are frequently discernible (B). A and B X130.

References

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PERICARDIAL CYST

SYNONYMS AND RELATED TERMS: Pericardial coelomic cyst; mesothelial cyst; hydrocele of the mediastinum; pericardial diverticulum.

Definition. These cysts of the parietal pericardium are identical morphologically to the pericardium and, occasionally, communicate with the pericardial space. They are uniformly benign and usually asymptomatic.

Clinical Aspects. The majority of patients with pericardial cysts are asymptomatic; the cysts are first noted either on a routine chest roentgenogram or as an incidental finding at necropsy. However, as summarized in Table 14, slightly more than one-third of the patients with pericardial

TABLE 14

PERICARDIAL CYST
PRESENTING SYMPTOMS IN 82 PATIENTS

Symptoms	Number	Percent
Asymptomatic	48	59
Chest pain	18	22
Dyspnea	8	10
Persistent cough	3	4
Paroxysmal atrial tachycardia	2	5
Pneumothorax	1	
Hemoptysis	1	
Fever	1	
Total	82	100

cysts in the AFIP series were symptomatic. Chest pain, usually precordial or substernal, was the most frequent symptom. On chest roentgenogram, the cyst was rounded or elliptical, well demarcated, and of uniform density. Patients ranged from 4 to 83 years of age, although 62 percent were in their third and fourth decades at the time the cysts were discovered. Most series in the literature indicate a nearly equal incidence in males and females.

Description. Sites of the pericardial cysts in this series are summarized in Table 15. Pericardial cysts are most commonly found in the right heart border, usually at the right costophrenic angle (fig. 61). Nearly one-fourth of these cysts are present along the left heart border (fig. 62), and a small, but significant number (8 percent) project either into the anterior-superior or posterior mediastinum. Cysts range in size from 2 or 3 cm. up to 16 cm. or more in diameter. They are usually multilobulated on the external surface; however, the majority are unilocular, although the cyst lining is frequently trabeculated (fig. 63). In this series, 20 percent were multiloculated. They contain clear yellow fluid and, occasionally, communicate with the pericardial sac. A definite communication was visualized grossly in five of the cysts. The cyst wall is composed of connective tissue with abundant collagen and scattered elastic fibers and is lined by a flattened, single layer of mesothelial cells (fig. 64). Foci of hyperplastic mesothelial cells are occasionally encountered (fig. 65). Rarely, aggregates of lymphocytes and plasma cells and foci of calcification are present in the cyst wall.

Most authors agree that the pericardial cyst and pericardial diverticulum are one and the same. Persistent, blind-ending, parietal pericardial recesses seem the most plausible explanation for the origin of the pericardial cyst.

TABLE 15

PERICARDIAL CYST
LOCATION IN 82 PATIENTS

Site	Number	Percent
Right costophrenic angle	57	70
Left costophrenic angle	18	22
Anterior and superior mediastinum	4	4
Posterior mediastinum	3	4
Total	82	100

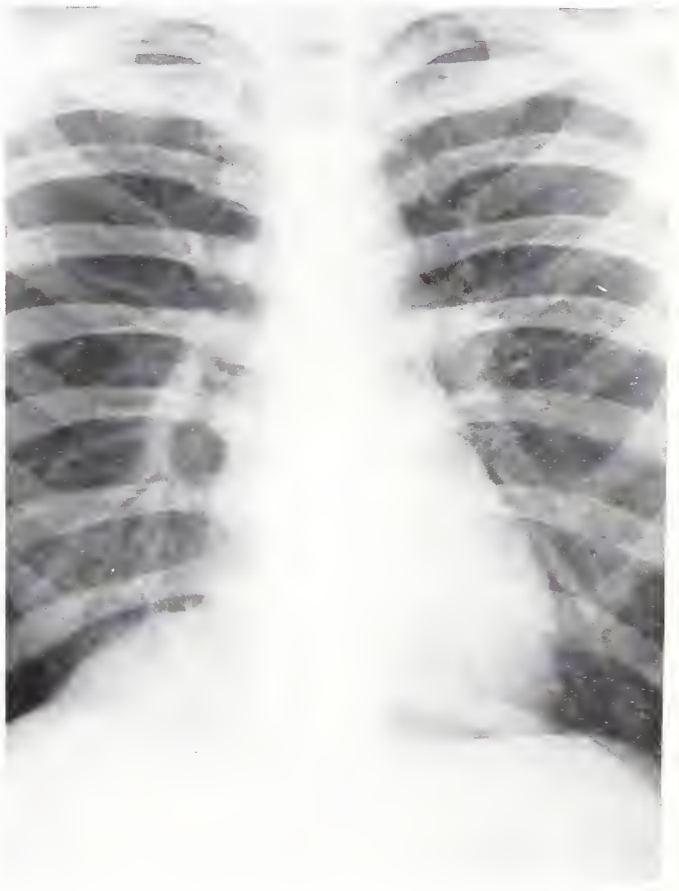

Figure 61
PERICARDIAL CYST
The typical appearance of a pericardial cyst at the right costophrenic angle is seen on this chest roentgenogram.

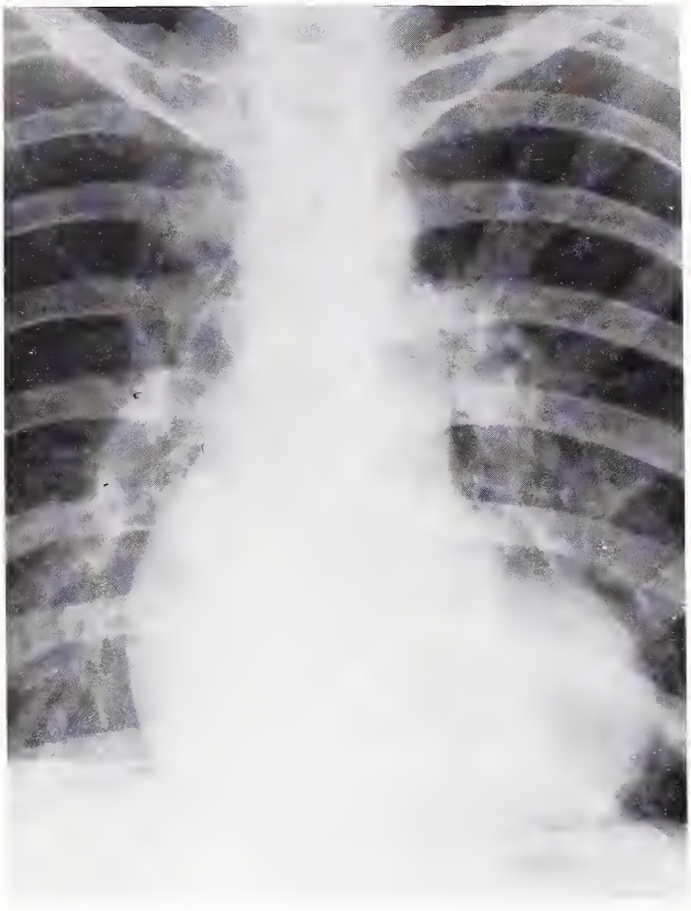

Figure 62
PERICARDIAL CYST
The typical appearance of a pericardial cyst at the left costophrenic angle is seen on this chest roentgenogram.

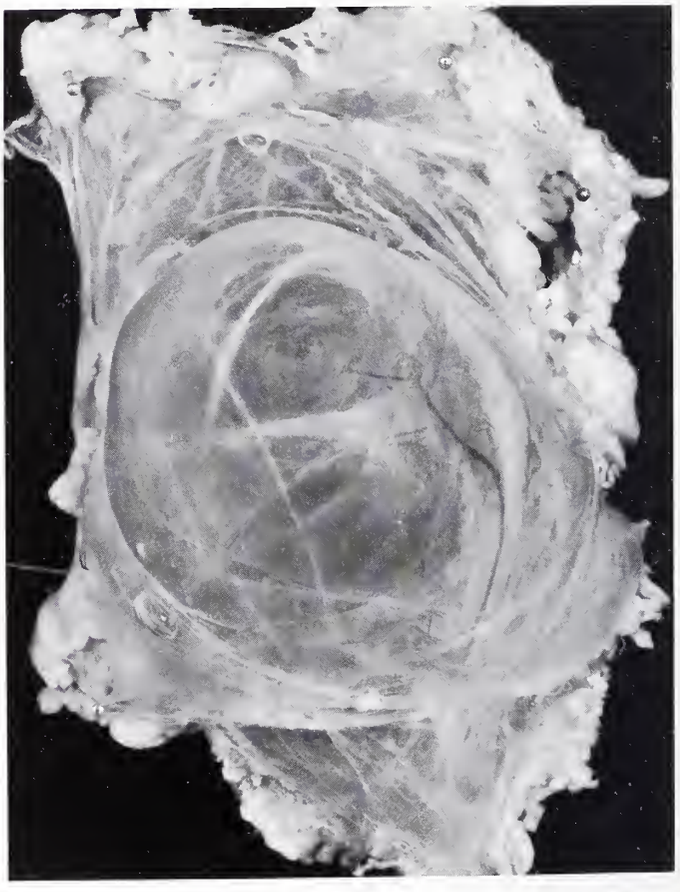

Figure 63
PERICARDIAL CYST
Pericardial cysts are thin-walled and translucent and filled with clear, pale yellow fluid. Although continuous with the pericardium, a communication with the pericardial cavity can be demonstrated in only a small percentage of cysts.

Figure 64
PERICARDIAL CYST
The cyst is lined by a single layer of mesothelial cells. The wall consists of dense fibrous tissue and occasionally contains aggregates of lymphocytes and plasma cells. X125.

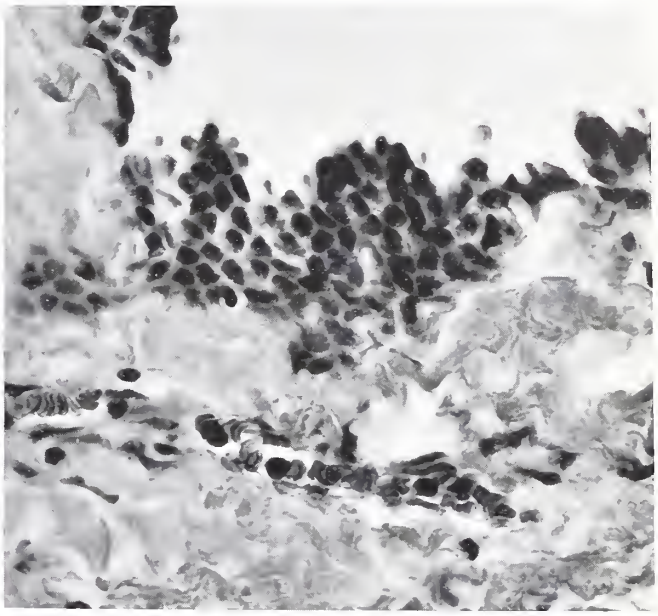

Figure 65
PERICARDIAL CYST
In the majority of pericardial cysts, focal areas of mesothelial hyperplasia are encountered. Tangential cuts such as this one will cause the mesothelial cells to appear "heaped up" and the nuclei large and hyperchromatic. This may occasionally present a diagnostic problem. X220.

Treatment. Four of the cysts in the AFIP collection were incidental findings at autopsy. Pericardial cysts were successfully excised from the 78 remaining patients. Thirty symptomatic patients experienced prompt relief of all symptoms; all 78 patients were alive and well, without evidence of recurrence or symptoms, at least two years following operation.

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Tumors Simulating Pericardial Cyst

Other tumors of the pericardium may simulate the clinical picture of a pericardial cyst. Four lipomas, one hemangioma, and one lymphangioma of the pericardium, in the AFIP collection, are discussed in their appropriate chapters. These tumors were located at the right or left costophrenic angle, and the clinical diagnosis for each patient was pericardial cyst. Ultrasonic diagnosis and computerized axial tomography may be helpful in differentiating pericardial cysts from solid tumors of the pericardium. Treatment and prognosis, however, are the same as for pericardial cysts.

OTHER BENIGN CARDIAC TUMORS

GRANULAR CELL TUMOR

A rare and apparently incidental tumor of the heart, the granular cell tumor has been found in the atria and on the epicardial surface and is frequently multiple. Histologically, it is identical to granular cell tumors elsewhere in the body, and we know of no solid evidence to suggest that these tumors are derived from striated muscle. In reported cases these tumors are mere oddities of no clinical significance, but they have been commonly mistaken for rhabdomyomas.

There are three adult patients with granular cell tumor of the heart in the AFIP collection. In each patient, the tumor was originally diagnosed as rhabdomyoma. In our experience, rhabdomyomas are very uncommon in adults. As previously discussed, granular cell tumors, as well as lipomas and fibromas with entrapped muscle, must be excluded before diagnosing cardiac rhabdomyoma in an adult. Individual cells which comprise the granular cell tumor are rounded or elongated (figs. 66, 67); they are filled with cytoplasmic granules that stain red with Masson trichrome stain, and exhibit a positive reaction with PAS that is unaffected by prior diastase digestion.

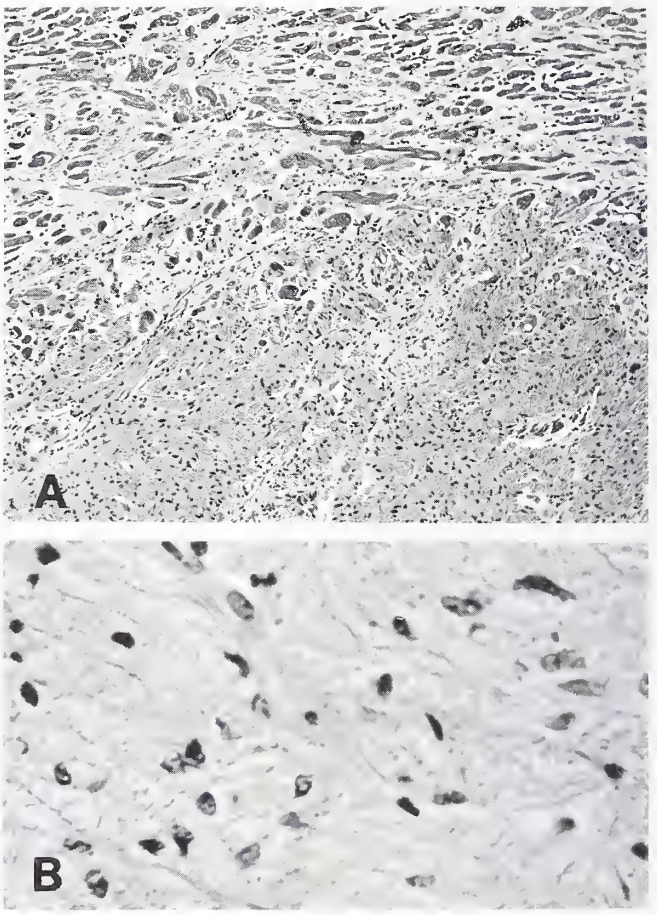

Figure 66
GRANULAR CELL TUMOR

A. The cells in this granular cell tumor in the right atrium are compact and filled with cytoplasm, unlike the large vacuolated cells of the rhabdomyoma with which the granular cell tumor is frequently confused. X50.

B. At high magnification, the granular nature of the cytoplasm is readily apparent—hence, the term granular cell tumor. Masson's trichrome stain, X375.

HAMARTOMA

Approximately 12 primary cardiac tumors, composed of more than one type of mesenchymal tumor, have been reported. Anbe and Fine reviewed these tumors and concluded that all but two were, in fact, lymphangiomas of the heart. The two exceptions were considered best classified as arterial or venous malformations, i.e., vascular hamartomas.

HETEROTOPIC TISSUE

Heterotopic islands of thymic tissue (fig. 68) and thyroid (fig. 69) have been described in the parietal pericardium. Thyroid rests have also been reported in the heart,

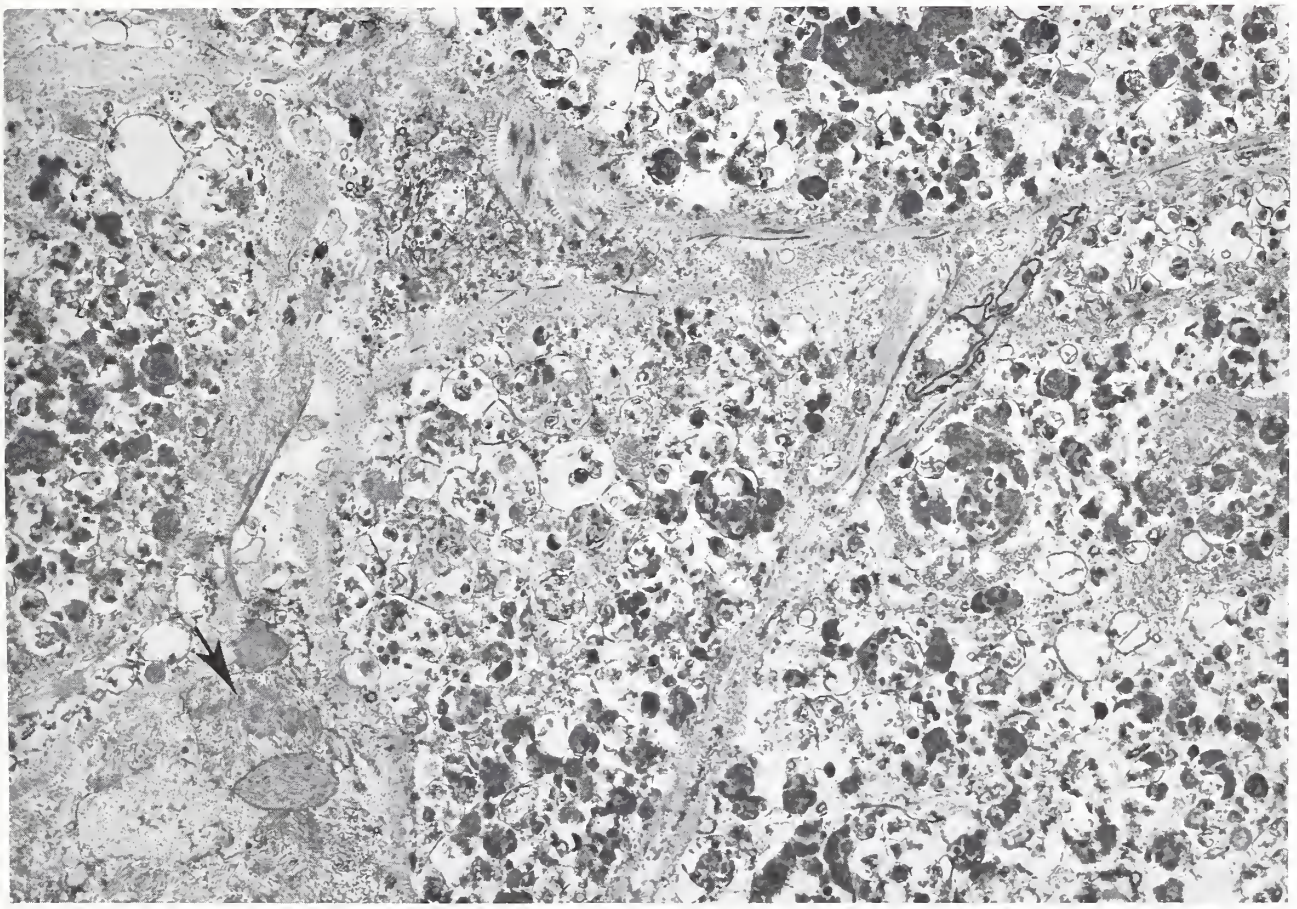

Figure 67
GRANULAR CELL TUMOR

Ultrastructurally, the cells of the granular cell tumor are filled with electron-dense granules which appear to be membrane bound. Other cells contain packets of microtubules called angulate bodies (arrow). No structures suggestive of striated muscle are identified. Uranyl acetate and lead citrate stain, X5775. (From Fenoglio, J. J. and McAllister, H. A. Granular cell tumors of the heart. Arch. Pathol. Lab. Med. 100:276-278, 1976.)

but, to our knowledge, a thyroid carcinoma primary to the heart has never been reported.

LEIOMYOMA

Interestingly, in the material we have reviewed, there are no examples of this tumor arising in the heart, and a search of the literature has not yielded any report of cardiac leiomyoma. There is, however, one report of a leiomyoma arising in the parietal pericardium.

LYMPHANGIOMA

Lymphangiomas are proliferations of lymphatic channels without proliferations of blood carrying channels (fig. 70). They are uncommon in the heart, but, as else-

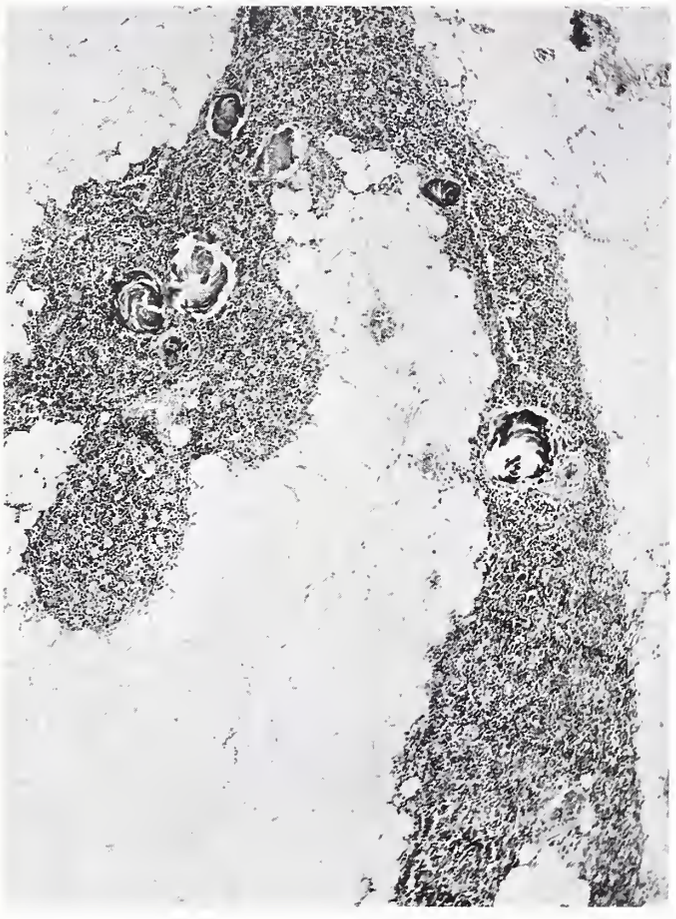

Figure 68
HETEROTOPIC THYMUS
This heterotopic thymus was located in the epicardial fat of the heart. X55.

where in the body, are frequently diffuse proliferations rather than distinct tumors. There are two cardiac lymphangiomas in the AFIP collection—one in the parietal pericardium and one in the left ventricular myocardium. Lymphatic ectasia, which may occur in the heart, must be distinguished from lymphangioma. So-called lymphangioendotheliomas of the atrioventricular node are discussed under mesothelioma of the atrioventricular node.

NEUROFIBROMA

Although exceedingly uncommon, neurofibromas have been reported in the heart, especially as a complication of von Recklinghausen's disease. In the AFIP collection, there were three neurofibromas involving the heart—one in the parietal pericardium and two in the left ventricular myocardium. Two of the patients had von Recklinghausen's disease; the third had a neuroblastoma during childhood, treated with radiation. Neurofibromas have also been reported in the right ventricle. Neurofibromas that occur in the heart are identical, grossly and microscopically, to neurofibromas elsewhere in the body.

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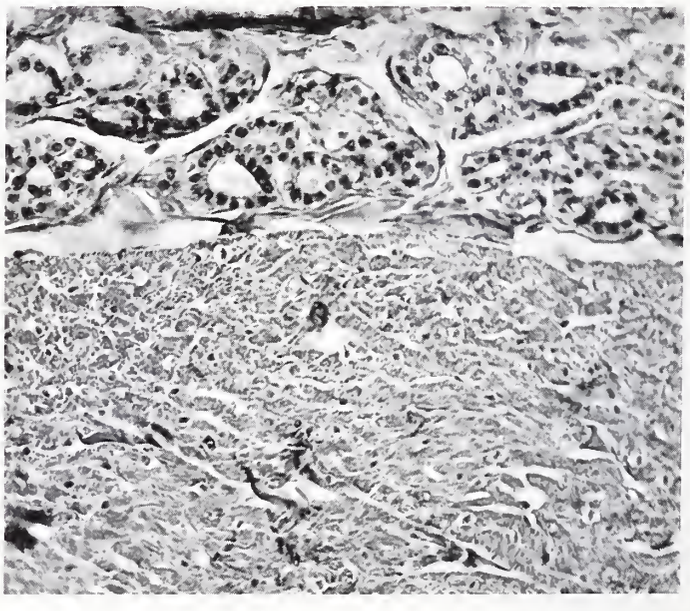

Figure 69
THYROID REST
A thyroid rest was located in the ventricular septum of a dog. Heterotopic thyroid tissue has also been reported in the human heart. X115.

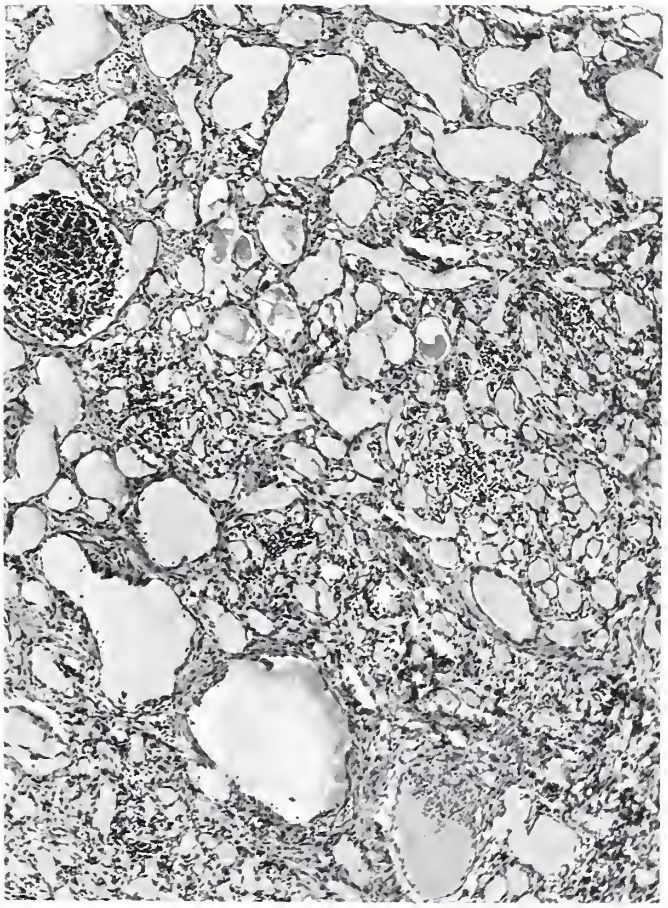

Figure 70
LYMPHANGIOMA

Lymphangiomas of the heart are uncommon. The tumor is composed of varying sized, thin-walled channels lined by flattened endothelial cells. The channels are filled with homogeneous proteinaceous material. X50.

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MALIGNANT TUMORS OF THE HEART AND PERICARDIUM

MESOTHELIOMA

SYNONYMS AND RELATED TERMS: Celothelioma; endothelioma; sarcoendothelioma; pericardial sarcoma.

Definition. Mesotheliomas are malignant tumors of the pericardium, either visceral or parietal, derived from mesothelial cells. By definition, we have included in this category only tumors confined to, or clearly originating from the pericardium that fulfill the established histologic, histochemical, or ultrastructural criteria. We prefer to classify so-called benign mesotheliomas of the pericardium as reactive mesothelial hyperplasia.

Morphologic Criteria. Microscopically, the mesothelioma is characterized by cellular regularity and histologic variability. Histologically, the tumor may be composed of tubules (figs. 71, 72) or solid cords of malignant cells that imitate the appearance of epithelium, or spindle-shaped cells that imitate fibroblasts (fig. 73) with an accompanying connective tissue stroma. Not infrequently, both patterns are present. Irrespective of the histologic pattern, the cells are usually remarkably regular in appearance (fig. 74). The cell size is variable but cellular pleomorphism and anaplasia are extremely unusual (fig. 75). Most frequently, the nuclei are large, rounded, and vesicular, with prominent nucleoli. The rounded, vesicular nuclei are often present, even in the predominantly spindle-cell or fibrous mesotheliomas. Atypical mitoses are rare, although multinucleated cells and occasional mitoses may be seen.

Histochemically, the vast majority of mesotheliomas (in our experience, all mesotheliomas) exhibit a positive staining reaction, either with colloidal iron or alcian blue (pl. V-A). Both intracellular and intercellular positivity is present, although the extent and intensity of the positive staining reaction may be variable, especially in predominantly fibrous mesotheliomas. Prior hyaluronidase digestion uniformly abol-

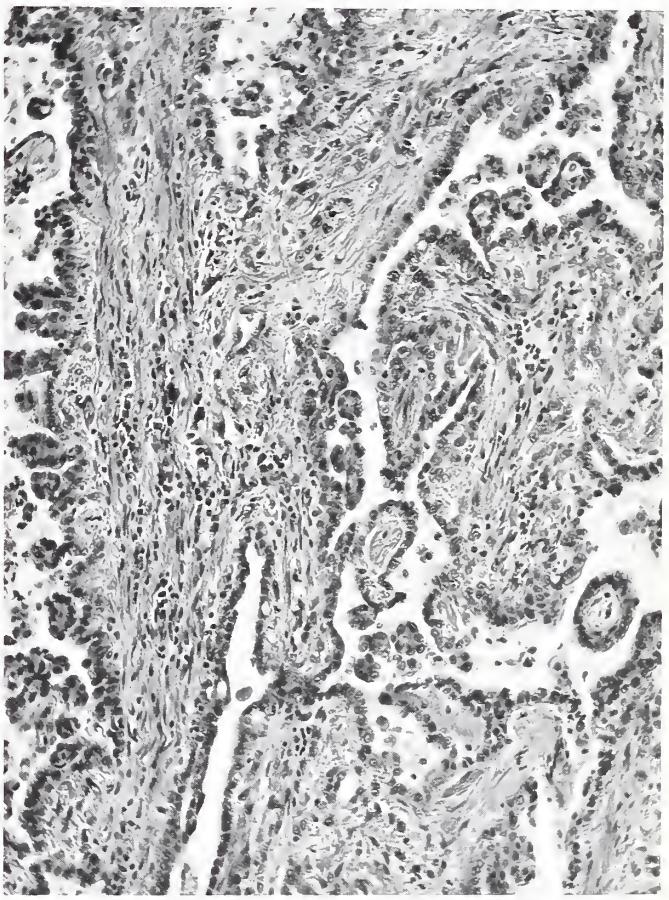


Figure 71
MESOTHELIOMA
Papillary areas are usually encountered in the mesothelioma. In these areas, the stroma is abundant and the fronds are covered by a single layer of mesothelial cells. X130.

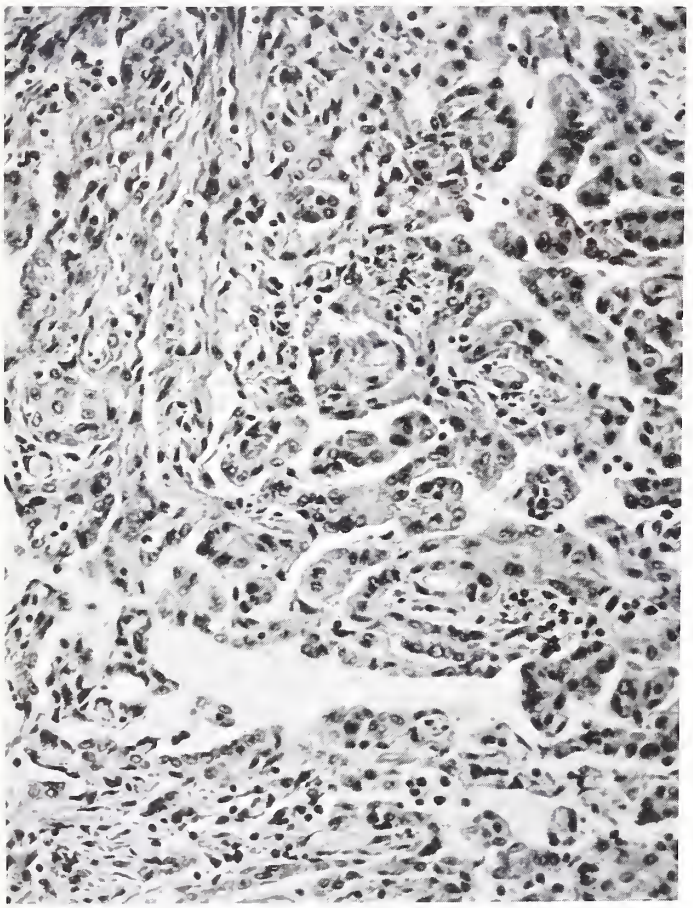


Figure 72
MESOTHELIOMA
Tubular and tubulopapillary areas are characteristic of the mesothelioma. Usually solid, papillary, and tubular areas are admixed within a single tumor. X180.

ishes, or markedly diminishes the positive staining reaction with colloidal iron or alcian blue (pl. V-B). The periodic-acid Schiff (PAS) reaction may be positive, but is generally negative following diastase digestion. Occasionally, PAS positive intracellular granules remain after diastase digestion; rarely, small intercellular foci of PAS positive diastase resistant material may be encountered. Although the stroma may occasionally stain weakly with mucicarmine stains, intracellular and luminal intercellular staining is uniformly negative.

Ultrastructurally, the surface membrane of the mesothelioma cell is covered by complex, irregular microvilli or globular cytoplasmic projections. The cells are joined at numerous points of contact by specialized junctions, frequently of the desmosome type. There are frequent intercellular spaces usually bounded by specialized junctions. The membranes of the intercellular spaces, as well as crypts within the cell cytoplasm, also have numerous microvilli. The cytoplasm contains a well developed endoplasmic reticulum, lipid droplets, glycogen granules, and, frequently, areas of fine microfilaments. Occasionally, intracytoplasmic and supranuclear cilia are identified.

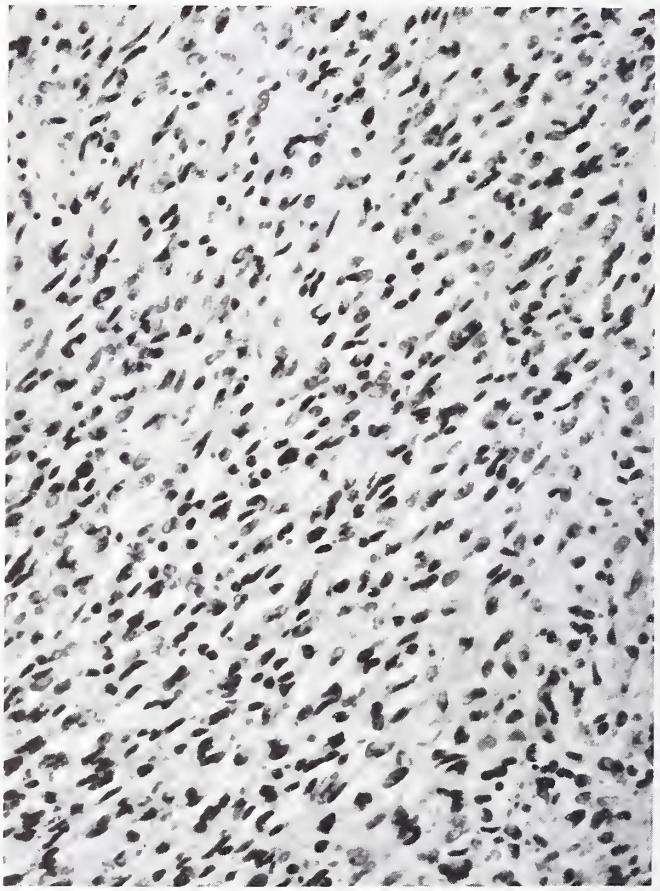
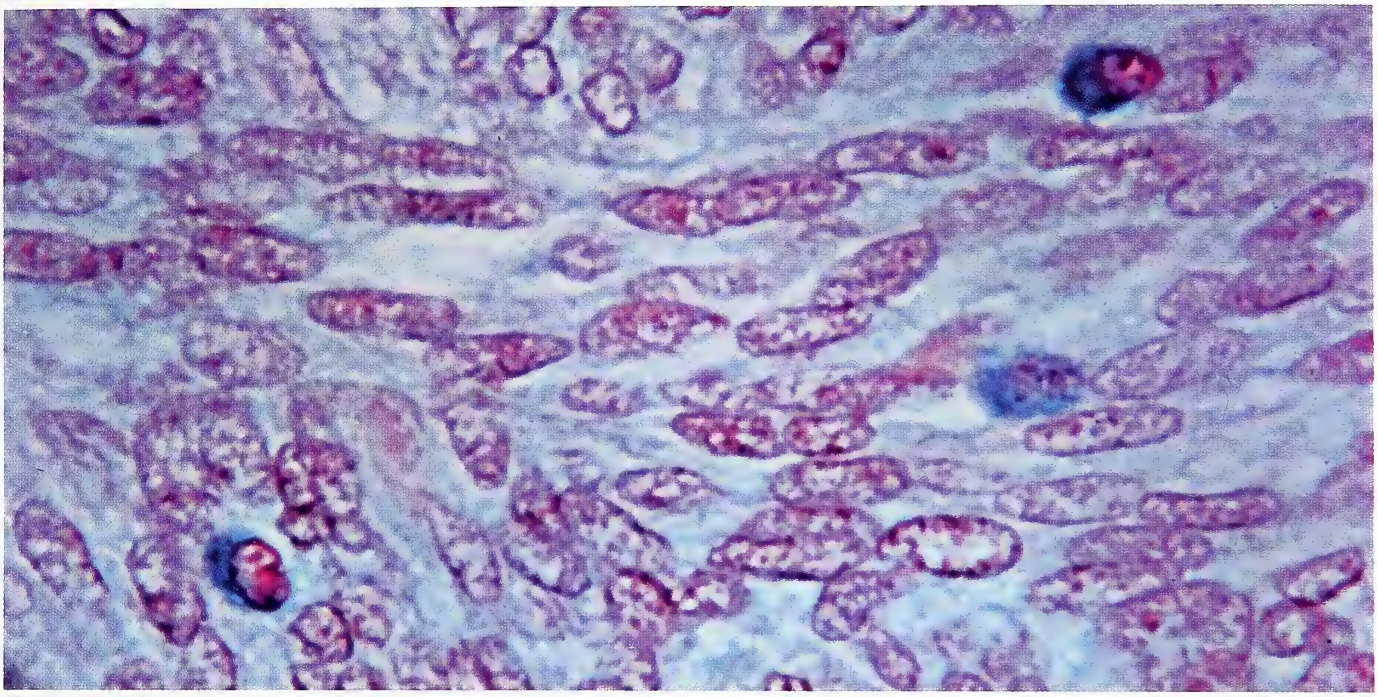


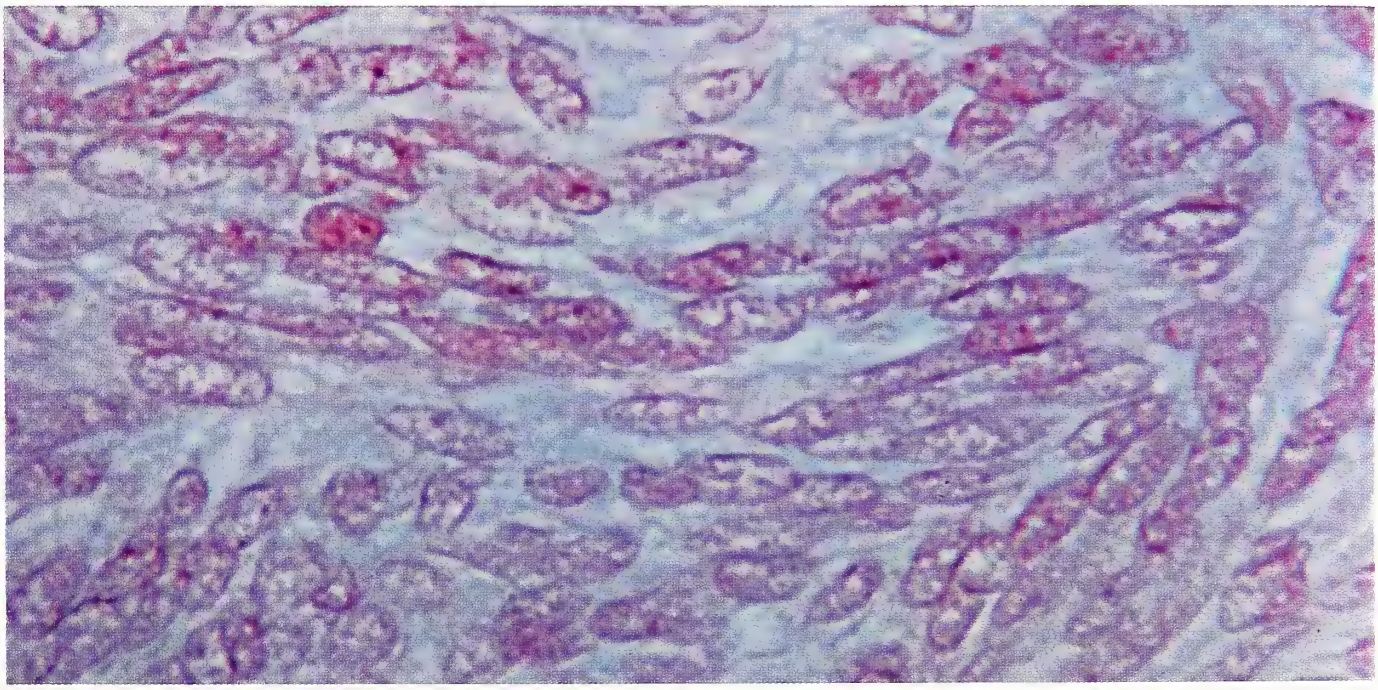
Figure 73
MESOTHELIOMA
The majority of pericardial mesotheliomas are composed, at least in part, of spindle-shaped cells that imitate fibroblasts; hence, the designation fibrous mesotheliomas. Although the cells are spindle-shaped, the nuclei are usually rounded and vesicular, with prominent nucleoli, unlike the elongated, blunt-ended nuclei of fibroblasts. X225.

PLATE V

MESOTHELIOMA



A. Intercellular and intracellular foci of alcian blue positive material are characteristic of mesothelial cells in general, and are found even in the cells of the fibrous mesothelioma. Alcian blue stain, X1150.



B. Characteristically, the positive alcian blue staining reaction is abolished by prior hyaluronidase digestion. This loss of intracellular alcian blue positivity following hyaluronidase digestion is one of the diagnostic criteria of mesothelioma. Alcian blue stain with prior hyaluronidase digestion, X1150.

Clinical Aspects. Clinical findings of the 19 patients in the AFIP series are summarized in Table 16. Dyspnea, usually with cough and signs of pericardial effusion, is the most common finding. Frequently, pericardial effusion is recurrent, and cytology on the aspirated fluid may be of diagnostic value. Many patients have symptoms of pericarditis and nonspecific S-T segment and T wave changes on electrocardiogram. Clinical findings of pericarditis and pericardial effusion are often present in these patients without a history or accompanying signs of an inflammatory disease. Other patients have signs and symptoms of constrictive pericarditis, often with severe right-sided congestive heart failure. Occasionally, the only clinical findings are fever, malaise, and weight loss. Cardiomegaly may be present on chest roentgenogram.

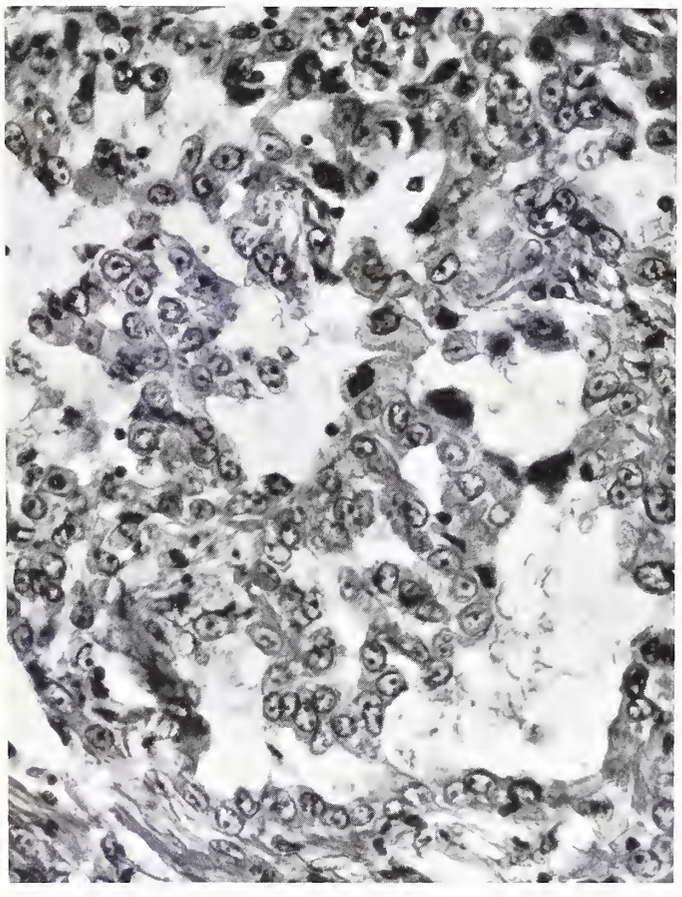


Figure 74
MESOTHELIOMA

At higher magnification, one may readily see the cellular regularity of the mesothelial cells of which the mesothelioma is comprised. Characteristically, the nuclei are large and vesicular and nucleoli are prominent. Mesothelial cells tend to keep these nuclear characteristics irrespective of the histologic pattern, and this is often a helpful feature in the differential diagnosis of mesothelioma. X300.

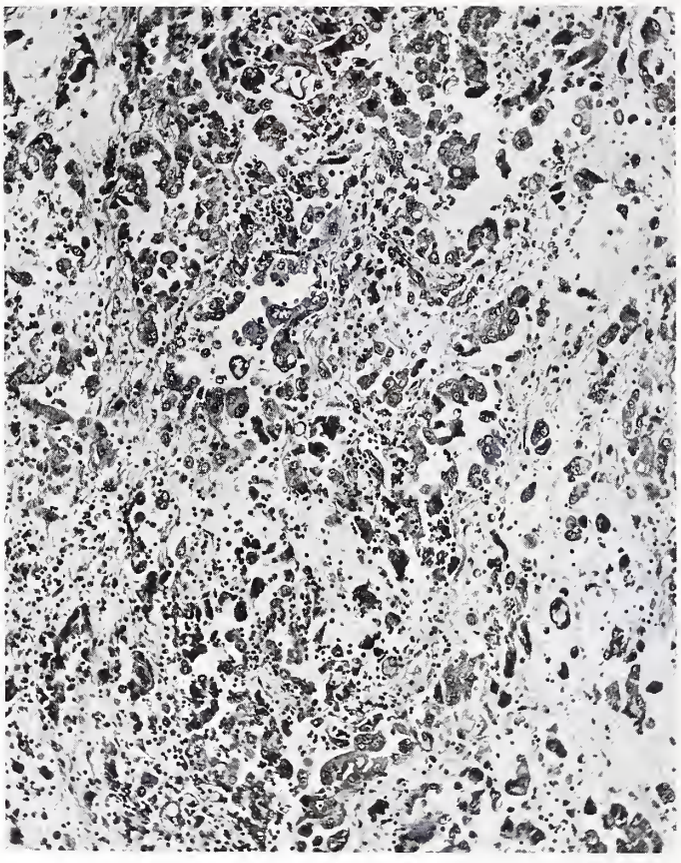


Figure 75
MESOTHELIOMA

Areas of apparent disorganization are present in all mesotheliomas. In these areas, the cells are arranged in nests and irregular groupings without obvious papillary or tubular formations; the intervening stroma is usually abundant. Multinucleated mesothelial cells are often abundant in these less well differentiated portions of the mesothelioma; however, nuclear atypia, although present, is not marked. X85.

Patients in the AFIP series ranged in age from 17 to 83 years. There were no children in this series, but mesotheliomas have been reported in the pediatric age group. The occurrence of mesotheliomas in children is unusual; in 1964, Kauffman and Stout accepted only 11 cases of malignant

mesothelioma in children. Most series indicate a male to female incidence ratio of nearly 2 to 1.

Description. Most mesotheliomas of the pericardium are diffuse and cover both the parietal and visceral pericardium. They may be sheetlike or nodular in appearance and almost invariably encase the heart, often apparently constricting the great arteries and veins as they enter or leave the heart (fig. 76). The mesothelioma grows by direct extension to surrounding surfaces and may superficially invade contiguous tissues. The epicardial myocardium was focally invaded (fig. 77) in many of the patients in the AFIP series, but the tumor did not extend to the endocardium or enter a cardiac chamber. This is an important differential point at the time of necropsy. Diffuse pericardial involvement can occur with other primary cardiac sarcomas, most notably angiosarcoma. Almost invariably, in addition to the pericardial involvement, other sarcomas of the heart have an intramyocardial or intracavitary component, whereas mesotheliomas only rarely, if ever, involve the cardiac chambers. The burden of proof whether a tumor that is both intracavitary and pericardial is a mesothelioma rests on the pathologist. Similarly, other cardiac sarcomas can be confined to the pericardium. These are usually easily distinguished from mesotheliomas by using the aforementioned morphologic criteria.

Solitary or, preferably, localized mesotheliomas do exist, but are uncommon (fig. 78). A localized mesothelioma is confined to one area of the pericardium, but usually involves both the parietal and visceral pericardium; in addition, it often has an intrapericardial component. Histologically, a localized mesothelioma is identical to a diffuse mesothelioma and may be of epithelial or fibrous type.

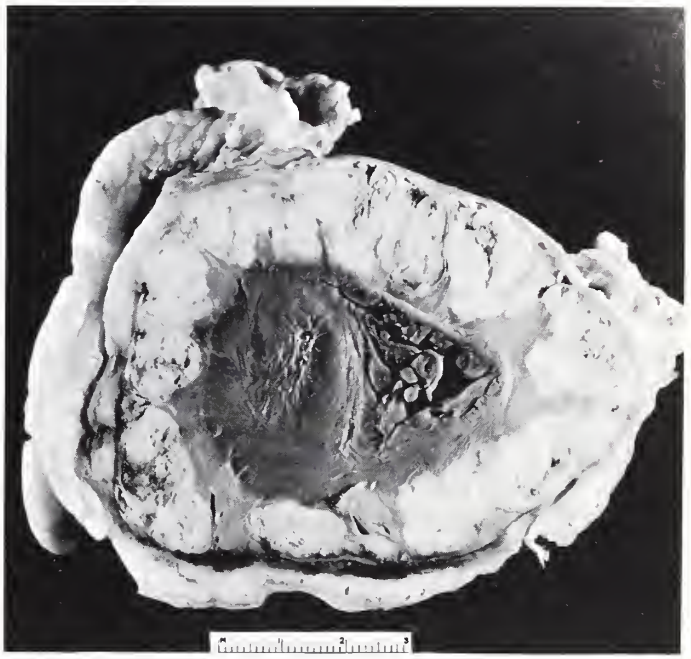


Figure 76
MESOTHELIOMA

The majority of pericardial mesotheliomas involve both visceral and parietal pericardium diffusely. The tumor often appears to encase the heart, and the myocardium is only rarely invaded. The sparing of the myocardium helps to distinguish mesothelioma from other sarcomas that occasionally involve the pericardium diffusely.

TABLE 16

MESOTHELIOMA OF THE PERICARDIUM
CLINICAL FINDINGS IN 19 PATIENTS

Findings	Number of Patients
Dyspnea	12
Pericardial effusion	11
Pericardial friction rub	7
Chest pain, pleuritic	6
Congestive heart failure	5
Cardiomegaly by roentgenogram	5
Fever	4
Low voltage on electrocardiogram	3
Sinus tachycardia	2
Paradoxical pulse	2
Weight loss	2

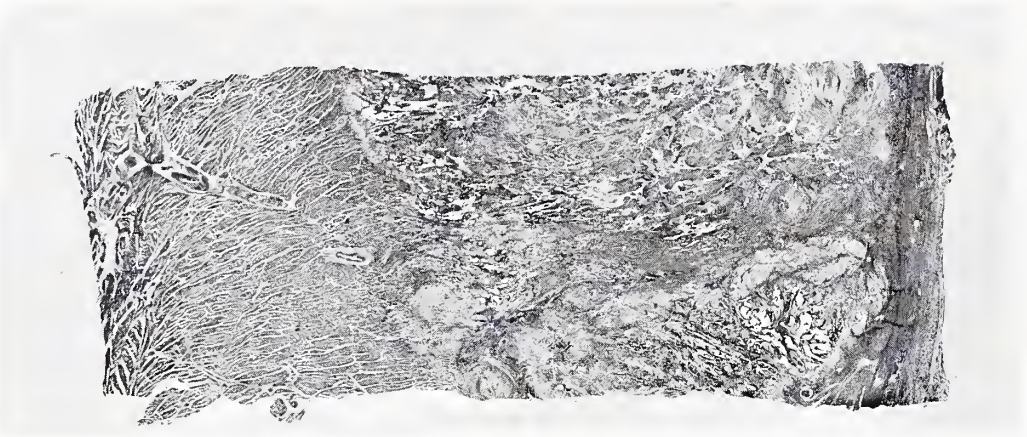


Figure 77
MESOTHELIOMA

Mesothelioma tends to obliterate the pericardial space and may actually constrict the heart, causing symptoms of constrictive pericarditis. Occasionally, the parietal pericardium (on the left in this photomicrograph) is not invaded. The tumor may extend along vessels from the epicardium (visceral pericardium) into the heart, although the myocardium is usually not directly invaded. X5.

Figure 78
MESOTHELIOMA

Localized or solitary mesotheliomas are uncommon, but do occur. They are confined to one area of the pericardium and usually involve both the parietal and visceral layers focally, obliterating the pericardial space.

Fibrous or mixed fibrous and epithelial mesotheliomas predominate in the pericardium as they do in the pleura, and pericardial mesotheliomas are indistinguishable from pleural mesotheliomas. In many patients, there is such extensive pleural and pericardial involvement that at necropsy it is impossible to determine where the mesothelioma arose; therefore, these patients are not included in this series. In spite of the similar appearance of pleural and pericardial mesotheliomas, there is no evidence to link the isolated pericardial mesothelioma to asbestosis. In contradistinction, there is a high incidence of asbestosis in patients with pleural mesothelioma. When mesotheliomas spread, they involve the surfaces of contiguous structures primarily and only rarely invade the underlying organ or tissue. Pericardial mesotheliomas frequently spread to the adjacent pleura and mediastinum and may involve the mediastinal lymph nodes. Occasionally, pericardial mesotheliomas spread through the diaphragm and involve the peritoneum. Distant metastases are extremely unusual if, indeed, they do occur. Any suspected

mesothelioma with extensive distant metastases must be thoroughly and carefully evaluated.

Differential Diagnosis. Differentiation of metastatic carcinoma involving the pericardium from **mesothelial hyperplasia** and **mesothelioma,** especially on a pericardial biopsy, may be extremely difficult.

Mesothelial hyperplasia may be focal (fig. 79) or diffuse and is found most frequently in patients with underlying cardiac disease, i.e., chronic pericarditis or chronic rheumatic heart disease. The reactive mesothelial cells are usually extremely regular in appearance; however, they may be large with large vesicular nuclei and prominent nucleoli. Most frequently they appear epithelial-like. Tubular and tubulopapillary forms are common (fig. 80). The mesothelial cells may form tumor-like masses within the pericardial space. The cells are remarkably uniform in appearance with virtually no pleomorphism, with little or no intervening stroma (fig. 81). Spindle-cell foci of mesothelial cells are not a feature of

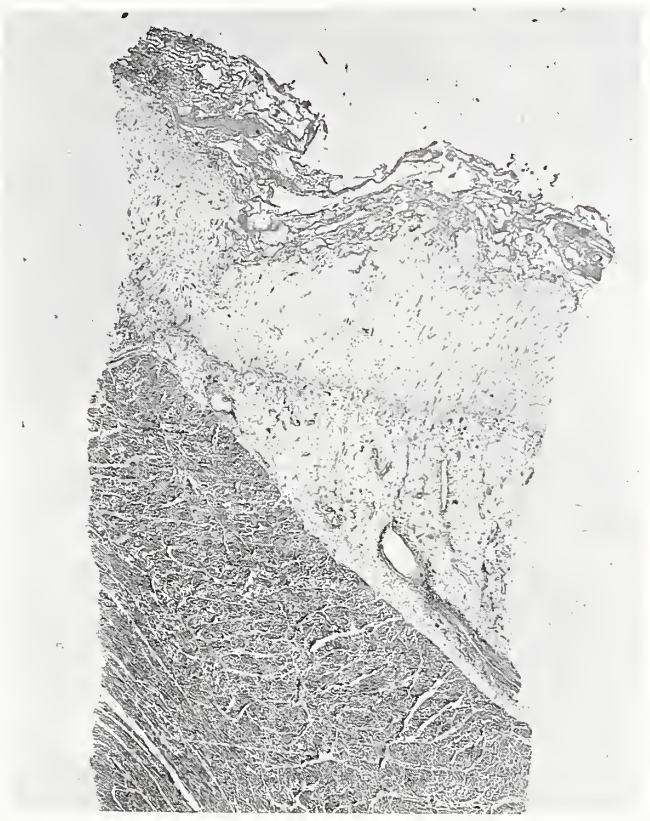


Figure 79
MESOTHELIAL HYPERPLASIA

Mesothelial hyperplasia is often diffuse, especially in patients with underlying cardiac disease. Usually, only the visceral pericardium is involved, covered by multiple fronds and clusters of mesothelial cells. The parietal pericardium may be involved, and there are often adhesions between the parietal and visceral pericardium. In contrast to mesotheliomas, the pericardial space is not obliterated and the epicardial fat is not invaded. X6.

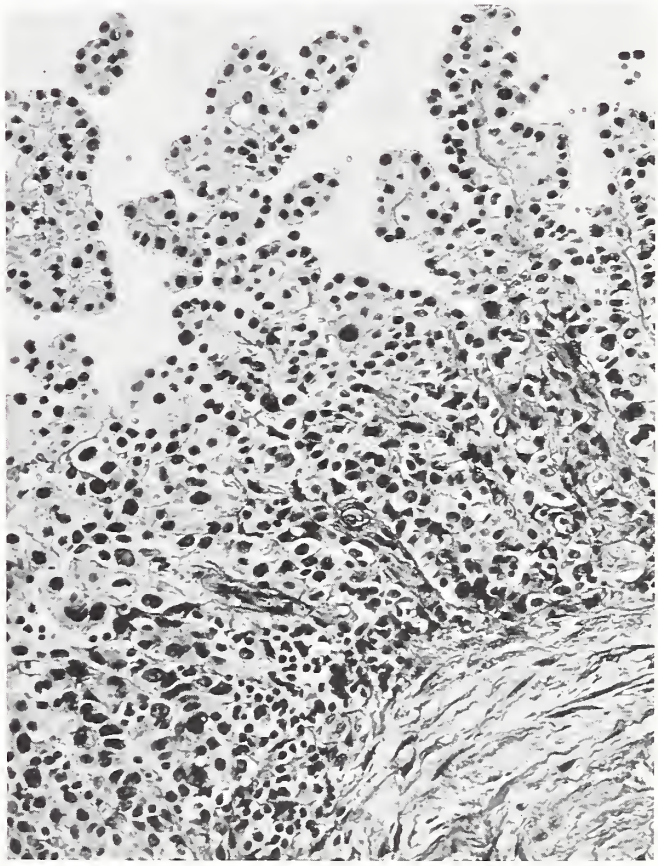


Figure 80
MESOTHELIAL HYPERPLASIA

The fronds and clusters of mesothelial cells on the surface of the pericardium characteristically lack an intervening fibrous stroma. The cells are usually bland and uniform in appearance. Rarely, nuclear atypia and mitotic figures may be present, and are not reliable indicators of benign or malignant tumor. Lack of invasion of the underlying pericardium and a scant or absent stroma between mesothelial cells indicate mesothelial hyperplasia, although islands of entrapped mesothelial cells may be present in fibrous pericarditis. X230.

mesothelial hyperplasia. More frequently, mesothelial hyperplasia is diffuse along the parietal or visceral pericardium. Reactive mesothelial cells are multilayered, and nests of mesothelial cells often lie within the pericardial stroma. Again, the cells are remarkably uniform in appearance, with minimal pleomorphism. Mitoses may be seen.

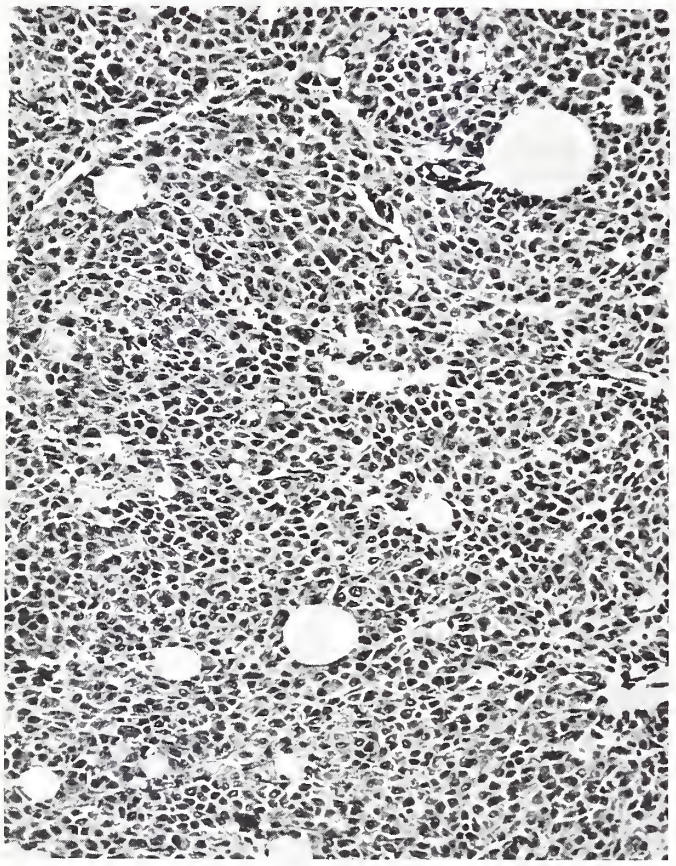


Figure 81
MESOTHELIAL HYPERPLASIA

Tumor-like masses of reactive mesothelial cells are also encountered. Usually, these aggregates of mesothelial cells are loosely attached to one of the layers of the pericardium and often associated with diffuse reactive mesothelial hyperplasia. Unlike mesotheliomas, these solid foci of mesothelial hyperplasia are usually histologically uniform. The entire mass is composed of sheets of mesothelial cells without papillary or tubular areas and there is usually little or no supporting stroma. Histologically, the differentiation between a solid area of mesothelioma and focal mesothelial hyperplasia on biopsy specimens is extremely difficult, and, therefore, the gross description is essential. X140.

Reactive proliferations of mesothelial cells exhibit the same staining characteristics as mesotheliomas, but the staining reactions are more intense. These staining properties differentiate mesothelial hyperplasia from metastatic carcinoma involving the pericardium. Many metastatic carcinomas stain positively, at least in part, with mucicarmine stain or with the PAS reaction after diastase digestion. Many carcinomas that are likely to be confused with mesothelial proliferations stain positively with colloidal iron or alcian blue; in metastatic carcinoma cells, this staining reaction is not abolished by prior hyaluronidase digestion, but is abolished in mesothelial cells. This differential special staining of mesothelial cells and carcinoma cells, together with the clinical history, should distinguish mesothelial hyperplasia from metastatic carcinoma involving the pericardium. Mesothelial hyperplasia may be a complication of treatment by radiotherapy for patients with carcinoma, or secondary to the pericarditis that may follow the spread of carcinoma to the pericardium. Finding only mesothelial hyperplasia in a patient suspected of having metastatic pericardial carcinoma, therefore, does not exclude the diagnosis of metastatic carcinoma involving the pericardium.

Distinction between **mesothelial hyperplasia** and **mesothelioma** is far more difficult. A prerequisite is a thorough knowledge of the morphologic spectrum of normal and hyperplastic mesothelial cells. The degree of pleomorphism, presence of anaplasia, extent of pericardial involvement, number of mitoses present, and presence of abnormal mitoses may all be helpful diagnostic aids, but these features, alone or together, do not necessarily establish a diagnosis of mesothelioma. The presence of spindle-cell foci of mesothelial cells is a more reliable indicator of a pericardial

mesothelioma. Spindle-cell foci are present in at least 50 percent of pleural and pericardial mesotheliomas in reported series and in 84 percent of the pericardial mesotheliomas in the AFIP series, while spindle-cell areas are extremely rare in reactive mesothelial hyperplasia or benign mesotheliomas (10 percent or less in most reported series).

Cytology. Exfoliative cytology has been used as an aid in the diagnosis of mesothelioma. The distinction between hyperplastic and malignant mesothelial cells is, however, extremely difficult. Routine exfoliative cytology is usually helpful in establishing the diagnosis of metastatic carcinoma of the pericardium.

Treatment. There is no specific treatment for pericardial mesothelioma. Surgical excision is usually not possible. Although radiotherapy and chemotherapy have been reported to produce temporary improvement, there is no correlation between this treatment and the course of the disease. Prognosis is generally poor; as many as 60 percent of patients die within six months of diagnosis, although survivals of five and six years have been reported.

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ANGIOSARCOMA

SYNONYMS AND RELATED TERMS: Angioendothelial sarcoma; malignant hemangioendothelioma; hemangioendotheliosarcoma; malignant hemangiopericytoma; hemangiosarcoma; malignant hemangioblastoma; hemangioendothelioblastoma; Kaposi's sarcoma.

Definition. Angiosarcomas are neoplasms comprised of malignant cells forming vascular channels. Angiosarcomas arising in the heart are rare, but are the most frequently occurring primary cardiac sarcomas. These tumors are often subclassified on the basis of their microscopic appearance; however, since their clinical course and prognosis appear to be identical, irrespective of the subclassification, we prefer the all inclusive term angiosarcoma.

Clinical Aspects. Clinical findings of the 39 patients in the AFIP series are summarized in Table 17. We have included only those patients in whom the heart was unequivocally the primary site or in whom metastases were small and did not involve the skin or soft tissues. Only 11 patients had distant metastases; in three, the metastases were confined to the central nervous system. Five additional patients had local spread of the tumor to the adjacent pleura and/or mediastinum. The largest mass of

TABLE 17

ANGIOSARCOMA OF THE HEART
CLINICAL FINDINGS IN 39 PATIENTS

Findings	Number of Patients
Congestive heart failure	15
Pleuritic chest pain, pericardial friction rub, dyspnea, fever	9
Dyspnea without pericardial findings	8
Pericardial effusion	7
Systolic murmurs	4
Anginal chest pain	4
Weight loss, fever, and malaise	4
Atrial fibrillation	3
Sudden unexpected death	2
Pulmonary emboli	1

tumor was in the heart of all 39 patients; all were adults, ranging in age from 15 to 76 years, although 70 percent were between 20 and 50 years. In this series, as in other published series, angiosarcomas are found 2 to 3 times more frequently in men than in women. The majority of patients in this series (77 percent) had clinical findings of right-sided heart failure or of pericardial disease. These findings included congestive heart failure, pericardial effusion, dyspnea, and pleuritic chest pain. A significant number of patients (10 percent), however, had symptoms suggestive of malignancy—fever, weight loss, and malaise—without cardiac findings or before cardiac findings were noted. Systolic murmurs and atrial arrhythmias were present in six patients; each of these patients also had evidence of right-sided heart failure. Cardiomegaly by chest roentgenogram and electrocardiographic abnormalities, nonspecific S-T segment and T wave changes and/or low voltage, were present in all patients.

Description. The right side of the heart or the pericardium was the site of origin of 80 percent of the angiosarcomas in this series (Table 18; pl. VI-A, B). In five patients, the extent of tumor involvement was so great that the primary site could not be determined; however, in each patient, the most extensive area of tumor involvement was the right side of the heart or the pericardium. An angiosarcoma arose from the left side of the heart in only three patients. There was right atrial and pericardial involvement in 11 patients; pericardial involvement was diffuse in 10 of the 11 patients and initially interpreted as mesothelioma. Special stains, especially alcian blue stains, with and without prior hyaluronidase digestion and reticulum stains, excluded the diagnosis of mesothelioma in each patient. In 10 patients, a portion of the tumor was intracavitary and partially obstructed a valve orifice. The tricuspid valve was most frequently obstructed by a right atrial tumor mass (seven patients), although the pulmonary valve was obstructed in two patients and the mitral valve in one.

TABLE 18

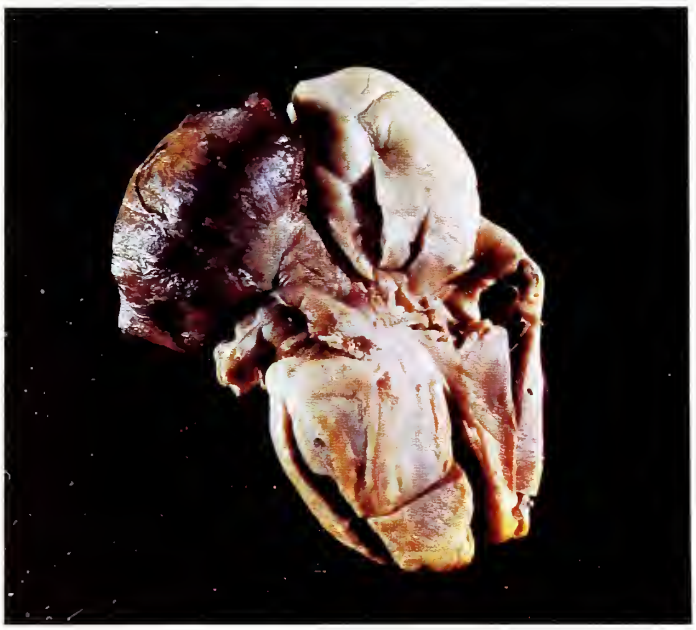
ANGIOSARCOMA OF THE HEART
LOCATION IN 39 PATIENTS

	Number of Patients	Primary Site*
Right atrium	39	25
Pericardium	15	4
Right ventricle	8	2
Left atrium	6	2
Left ventricle	5	1

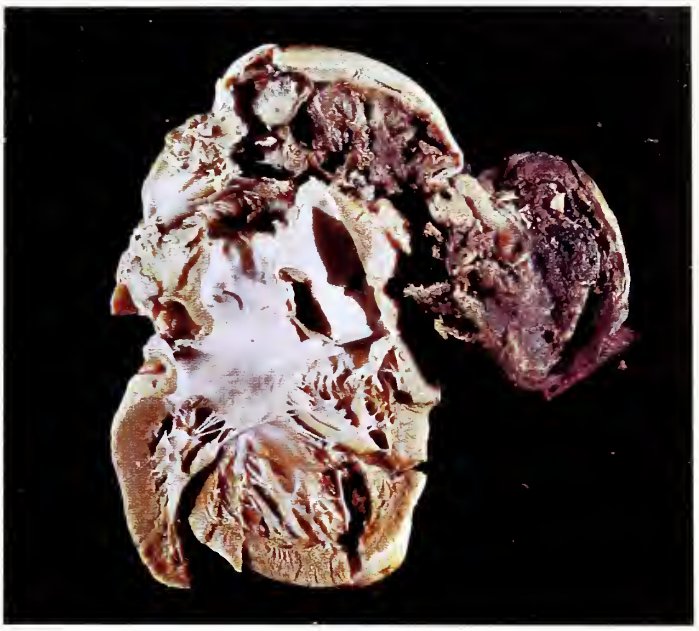
*Primary site could not be determined in 5 patients.

PLATE VI

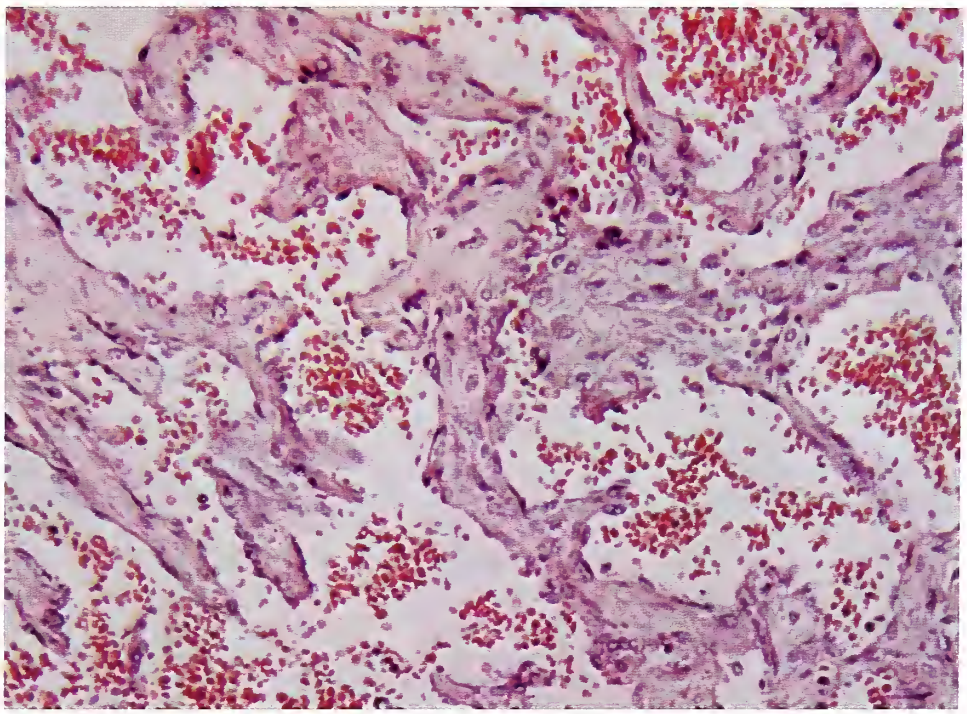
ANGIOSARCOMA
(Plate VI-A and B from same case)



A. Eighty percent of angiosarcomas of the heart arise in the right atrium or pericardium. In this patient, the right atrium is markedly distorted and the vascular nature of the tumor is apparent grossly.



B. On opening, the right atrial cavity is completely replaced and obliterated by the tumor which obstructs the tricuspid valve. In approximately 25 percent of patients in the AFIP series, a portion of the angiosarcoma was intracavitary and obstructed a valve orifice.



C. Multiple freely anastomosing vascular channels are characteristic of angiosarcomas and are helpful features in the differential diagnosis of benign and malignant vascular tumors. X105.

Microscopically, there is usually considerable variation in the appearance of an angiosarcoma, often within the same tumor. Basically, angiosarcomas are composed of abnormal proliferations of malignant cells forming vascular channels (pl. VI-C). Most of these tumors also contain foci of solid areas and spindle cells and, occasionally, they are composed almost entirely of sheets of rounded anaplastic cells or spindle cells (fig. 82). With a good reticulum stain, it is possible to demonstrate a vascular pattern in at least part of even the most cellular angiosarcoma. Trichrome stains and alcian blue stains are often helpful in differentiating angiosarcoma from mesothelioma and fibrosarcoma.

The vascular channels vary markedly in size and configuration, frequently with multiple anastomosing channels (fig. 83). The channels are lined by swollen, often multilayered, endothelial cells; these cells are rounded or elongated. Pleomorphism and anaplasia may be marked and mitoses are frequent. Tufting projections of heaped-up endothelial cells that lack an intervening stroma often project into the lumen of a vascular channel (fig. 84). Occasionally, endothelial cells fill the vascular channels giving the tumor a solid appearance. Reticulum stains will reaffirm the basic vascular pattern of these tumors. Spindle-cell areas frequently merge imperceptibly with vascular and solid areas of the tumor. The spindle cells are often blunt-ended and the nuclei are ovoid. Palisading is not prominent, and collagen production is minimal. Occasionally, vascular channels are not prominent and the solid areas are

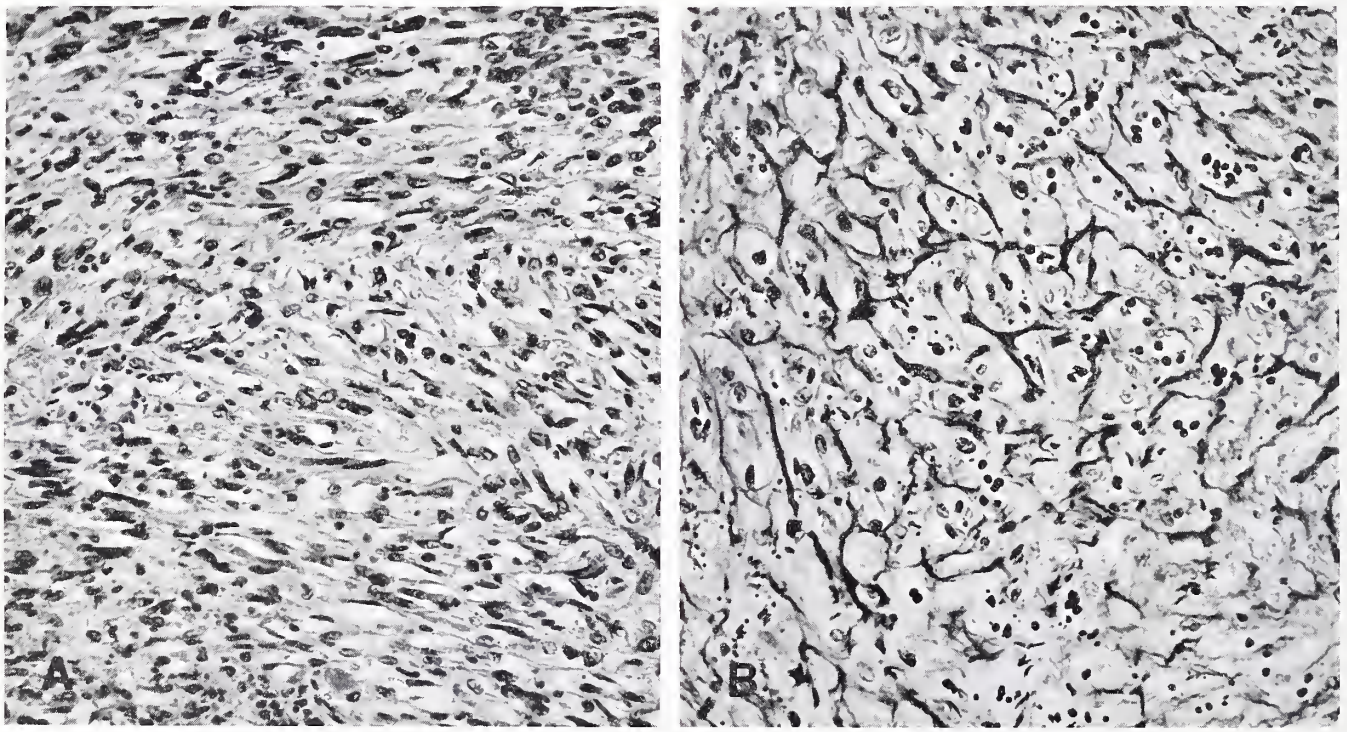


Figure 82
ANGIOSARCOMA

A. Foci of spindle cells, which often appear fibrosarcomatous, are frequent in angiosarcomas and often merge with vascular and solid areas. In these areas, the vascular pattern of the tumor is usually completely masked. X275. B. Reticulum stains are necessary to demonstrate the underlying vascular pattern. X275.

Panels A and B are from the same microscopic field of an angiosarcoma before and after reticulum staining.

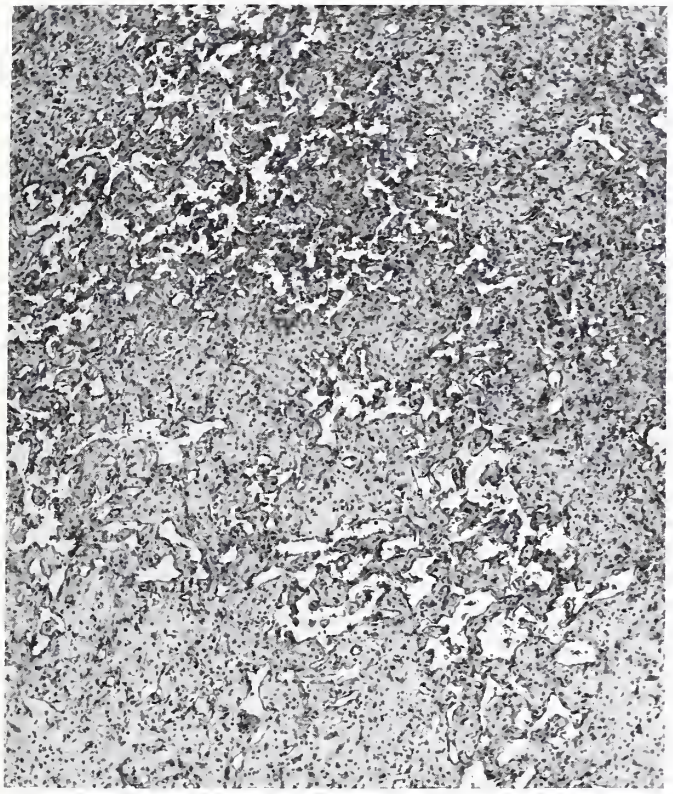


Figure 83
ANGIOSARCOMA

A solid phase of the tumor is frequent in angiosarcoma. Solid areas of the tumor often consist of rounded, swollen, endothelial cells which appear to fill the vascular channels. Such areas are frequently interspersed between the freely anastomosing vascular channels. Occasionally, however, large areas of the tumor appear solid, and the vascular pattern is only apparent with reticulum stains. X85.

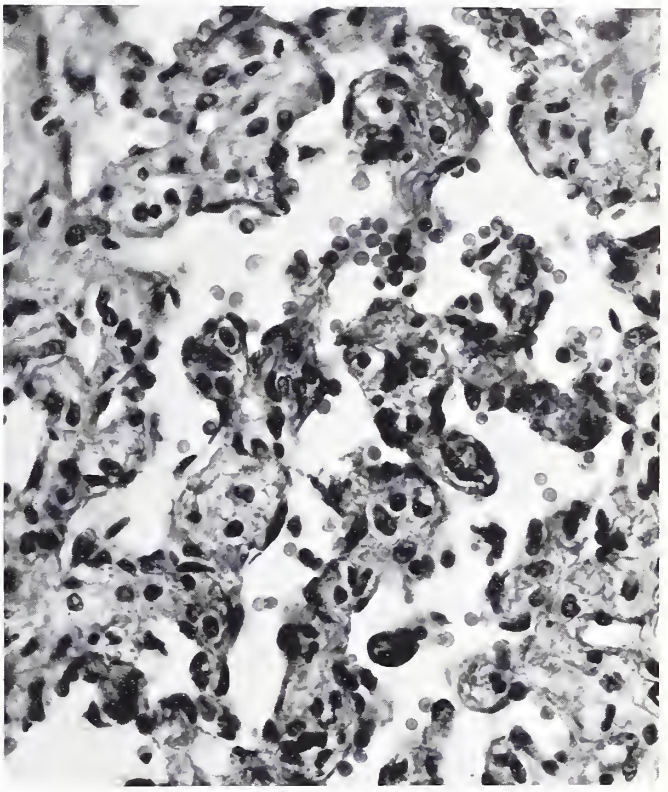


Figure 84
ANGIOSARCOMA

Tufting, or projections of clusters of endothelial cells into the vascular channels, is also a feature of angiosarcoma. The endothelial cells may be uniform with small ovoid nuclei or there may be marked cellular pleomorphism and nuclear atypia with abundant mitotic figures. Nuclear atypia and mitotic figures, although suggestive of malignancy, are not reliable diagnostic features in distinguishing between benign and malignant vascular tumors. X350.

composed of rounded or elongated cells, proliferating around a small vascular channel. This is the so-called hemangiopericytoma—a rare tumor. Only one angiosarcoma had the characteristics of a malignant hemangiopericytoma in our series (fig. 85), although foci suggestive of hemangiopericytoma were identified in at least half of the tumors.

Anastomosing vascular channels, foci of tufting, and spindle-cell areas are the most reliable indicators of a malignant vascular tumor. In combination with these features, pleomorphism, anaplasia, and mitoses are helpful diagnostic aids, but alone they are not reliable indicators of malignant tumor.

Much attention has been given to Kaposi's sarcoma of the heart, but only one tumor, confined to the pericardium, fulfilled the criteria of Kaposi's sarcoma in this series. By definition, Kaposi's sarcoma is a vascular tumor composed of vascular spaces between which are spindle-shaped cells and reticulum fibers resembling a well differentiated fibrosarcoma. Focal areas that fulfilled these criteria were present in many of the tumors in this series, and we feel that Kaposi's sarcoma, especially visceral Kaposi's sarcoma, is a variant of angiosarcoma.

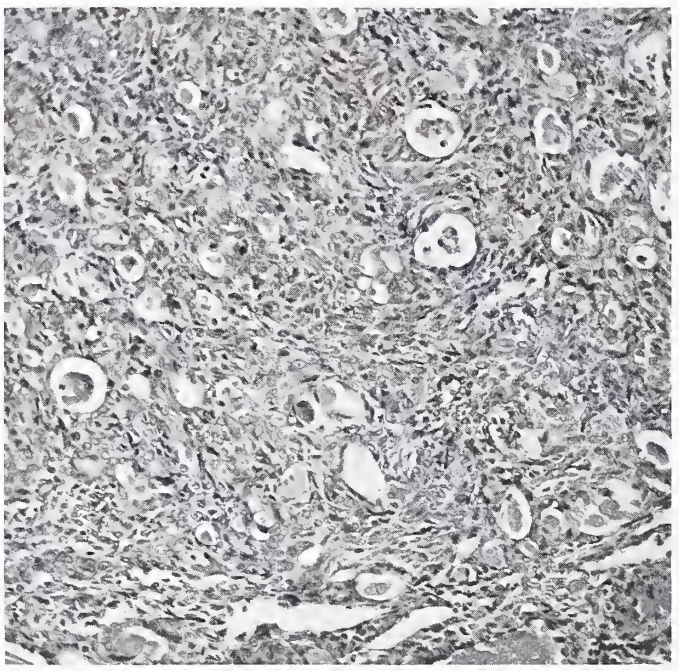


Figure 85
ANGIOSARCOMA

In many angiosarcomas, there are focal areas in which the cells proliferate around, rather than within the vascular channels. Reticulum stains confirm that the vascular channels are lined by a single layer of endothelial cells and that the proliferating cells lie outside the reticulin sheath of the vascular channel and, therefore, are pericytes. This is the morphologic picture of the hemangiopericytoma and was found focally in 50 percent of angiosarcomas. X130.

Ultrastructurally (fig. 86), angiosarcoma consists of large cells with numerous cytoplasmic processes, irregular cell borders, and numerous, intercellular, specialized junctions, usually of the desmosome or hemidesmosome type. Nuclei are irregular, nucleoli are prominent, and cytoplasmic vesicles and cytoplasmic inclusions, often of the myelin figure type, are frequently found. Abnormal endothelial cells that form complex, anastomosing channels and spaces are embedded in an extensive matrix of finely fibrillar and flocculent material. This matrix tends to condense into strata, forming complex, multilayered, basal lamina structures between nests of abnormal endothelial cells. Even in spindle-cell areas, specialized intercellular junctions and multilayered basal lamina structures are prominent.

Treatment.—Surgical excision is usually impossible because of frequent extensive pericardial involvement. Without treatment, prognosis is poor; the majority of patients die within a year after onset of symptoms. Radiation therapy and chemotherapy may offer some relief of symptoms. One patient was reportedly alive 10 months following such treatment, without progression of the primary tumor or of metastatic disease.

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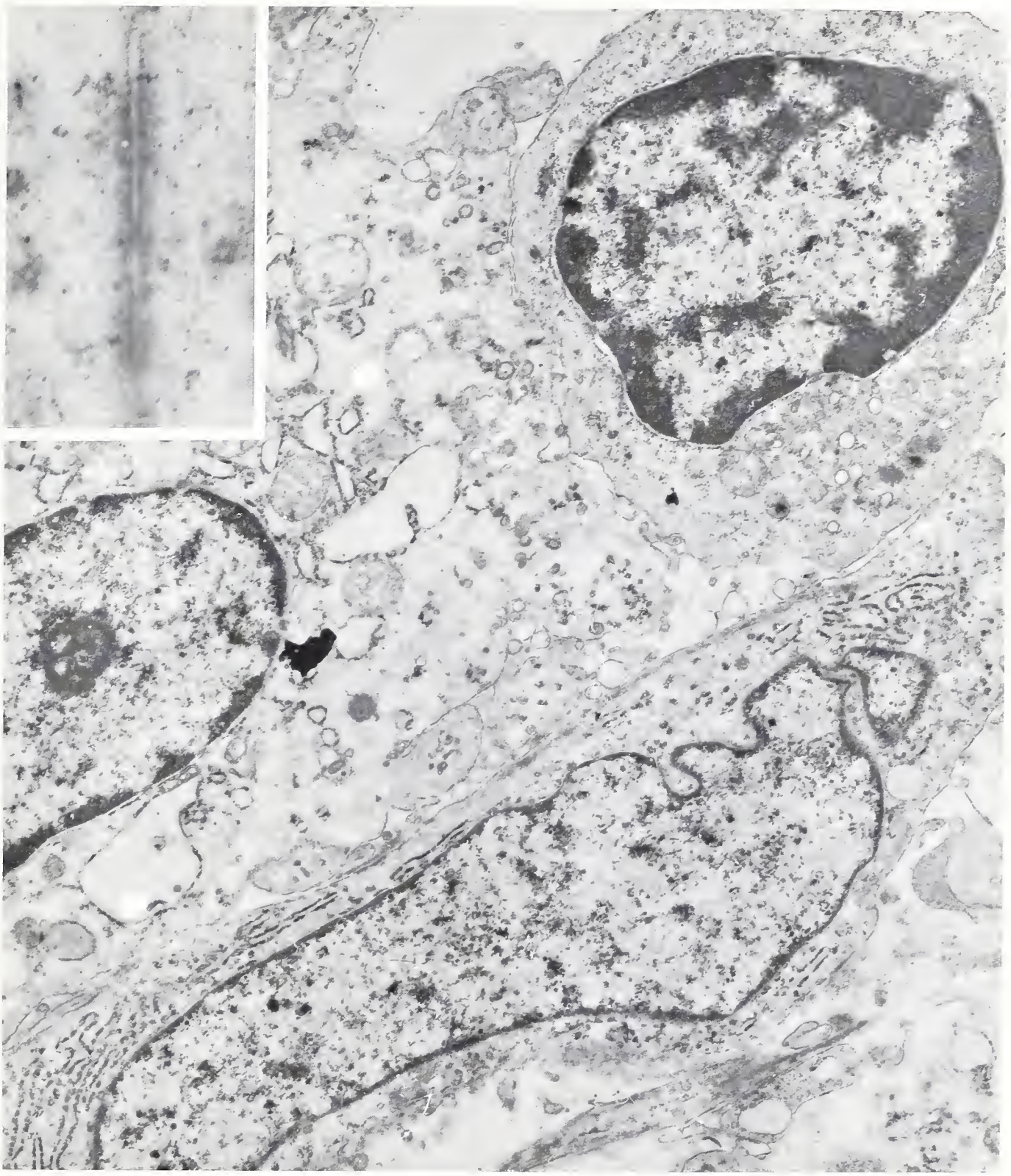

Figure 86
ANGIOSARCOMA

Ultrastructurally, cells of angiosarcomas are irregular in contour and have numerous cytoplasmic processes. The cells tend to line or form numerous channels which are often filled with red blood cells. The cytoplasm contains numerous cytoplasmic vesicles and abundant endoplasmic reticulum; pinocytotic vesicles frequently border the cell membrane. Uranyl acetate and lead citrate, X13,980.

Insert: The cells are variably joined at points of contact by specialized junctions of desmosome type. Uranyl acetate and lead citrate, X78,300.

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RHABDOMYOSARCOMA

SYNONYMS AND RELATED TERMS: Malignant rhabdomyoma; myosarcoma; embryonal rhabdomyosarcoma; alveolar rhabdomyosarcoma; rhabdomyoblastoma.

Definition. Rhabdomyosarcoma is a neoplasm comprised of malignant cells with features of striated muscle. It is the second most common primary sarcoma of the heart.

Clinical Aspects. In the AFIP collection, there are 26 rhabdomyosarcomas primary in the heart. Clinical findings of these 26 patients are summarized in Table 19. The tumor had metastasized in seven of these patients, involving other viscera only; in no patient was there soft tissue metastasis. The tumor was thought to be primary in the heart in each patient because the main tumor mass was located in the heart, or the metastasis was demonstrated to be embolic.

Rhabdomyosarcomas have been reported in patients ranging from three months to 80 years of age. In the AFIP series, ages ranged from 1 to 66 years, but only two patients were in the pediatric age group. The incidence of cardiac rhabdomyosarcoma in the adult population was nearly equal in all decades. A slightly increased incidence in men over women has been reported. The majority of patients in the AFIP series had nonspecific symptoms characterized by fever, anorexia, malaise, and weight loss—symptoms more indicative of malignancy than of cardiac disease. Findings of pericardial disease, pleuritic chest pain, pleural effusion, dyspnea, and embolic phenomena, both pulmonary and cerebral, were common in patients with rhabdomyosarcoma. Clinical findings were often confusing, leading to an incorrect diagnosis. A common denominator in all patients was cardiomegaly by chest roentgenogram and nonspecific electrocardiographic changes—S-T segment and T wave changes, low voltage, and/or varying degrees of bundle branch block. Most frequently, the heart borders were irregular and the contour of the heart was distorted. In addition, 50 percent of the patients had unexplained murmurs, usually systolic and of recent onset, and/or intractable atrial or ventricular arrhythmias. The combination

TABLE 19

CARDIAC RHABDOMYOSARCOMA CLINICAL FINDINGS IN 26 PATIENTS

Findings	Number of Patients
Weight loss, fever, malaise	11
Cardiac murmurs	10
Pericardial effusion, dyspnea, pleuritic chest pain	5
Sudden unexpected death	4
Embolic phenomena	4
Congestive heart failure	3
Atrial fibrillation	3
Ventricular arrhythmias	3
Cyanosis	2
Hemoptysis	2

of irregular cardiomegaly, nonspecific electrocardiographic findings, and cardiac murmurs or arrhythmias of recent onset is a clue to the possible presence of a cardiac tumor, even in the presence of findings indicative of other disease states.

Findings of impediment to blood flow, such as congestive heart failure, were common. Cardiac murmurs of changing intensity, a finding usually indicative of an intracavitary tumor (see pages 6 and 7), were not found. Nonetheless, in each patient in which a cardiac murmur was noted, a large portion of the rhabdomyosarcoma was intracavitary and there was significant obstruction of at least one valvular orifice.

Description. The number of tumors and their primary site of involvement within the heart are summarized in Table 20. Unlike angiosarcoma, there appears to be no propensity of rhabdomyosarcoma to arise in any one cardiac chamber. In 60 percent of the patients, the tumor involved multiple sites within the heart; in five patients, tumor involvement was so extensive that the primary site could not be determined. When the primary site could be determined, the tumor arose with equal frequency from the left and right sides of the heart (fig. 87). The pericardium was involved in 50 percent of patients, usually by direct extension of the tumor from the myocardium. Frequently, both the parietal and visceral pericardium were invaded. In five patients, the tumor extended beyond the parietal pericardium to the adjacent mediastinum or pleural cavity. Diffuse pericardial involvement, characteristic of mesothelioma or angiosarcoma, is not a feature of rhabdomyosarcoma. In 12

TABLE 20

CARDIAC RHABDOMYOSARCOMA
SITE OF INVOLVEMENT IN 26 PATIENTS

	Number of Patients	Primary Site*
Right ventricle	11	7
Left atrium	10	7
Right atrium	10	4
Left ventricle	6	3
Pericardium	13	

*Primary site could not be determined in 5 patients.

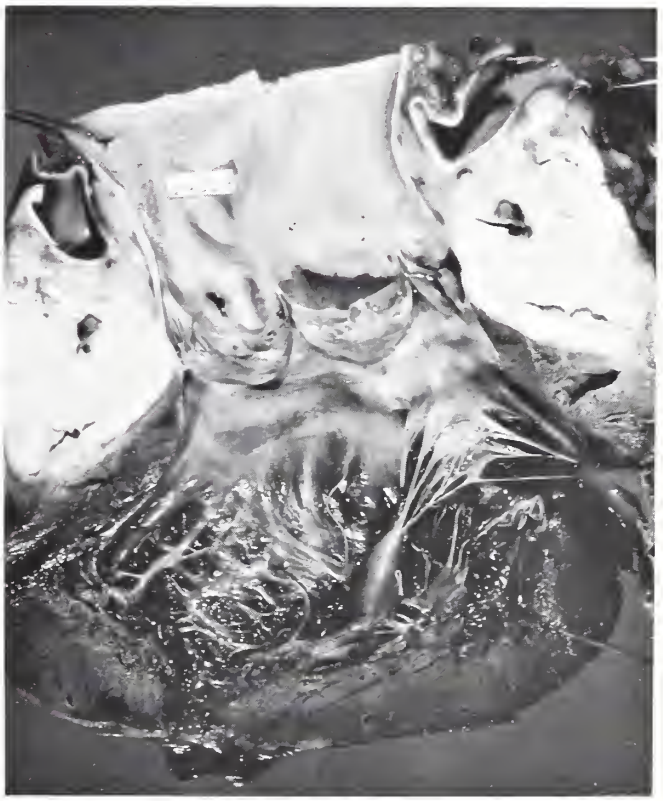


Figure 87
RHABDOMYOSARCOMA

Rhabdomyosarcomas arise with near equal frequency on the left and right sides of the heart and in the atria and ventricles. In this patient, the tumor arose in the left atrium and encased the base of the heart, trapping and compressing, but not invading the left coronary artery. The tumor extended to the right atrium but did not involve the ventricles. (From Cheitlin, M. D., deCastro, C. M., Knowles, D. M., Fenoglio, J. J., Jr., and McAllister, H. A., Jr. Clinical pathologic conference. Am. Heart J. 90:248-254, 1975.)

Figure 88
RHABDOMYOSARCOMA
Multiple sites of tumor involvement within the heart are common with rhabdomyosarcoma. As illustrated, multiple tumor nodules were found in this patient, not only in the right atrium and ventricle but also in the left ventricle and on the pericardium. A primary site within the heart could not be determined.

patients, a large portion of the tumor was intracavitary, with partial obstruction of at least one valve orifice. The mitral and pulmonic valves were involved most frequently, but occasionally there was involvement of the tricuspid valve and the aortic valve. Unlike benign intracavitary cardiac tumors, especially myxomas, intracavitary rhabdomyosarcomas often invaded or partially replaced the obstructed cardiac valves.

A portion of this tumor is always intramyocardial, even when there is an intracavitary component (fig. 88). Rhabdomyosarcomas are usually nodular, soft, and often centrally necrotic. Microscopically, both juvenile forms (embryonal or alveolar) and adult forms occur, the adult form much more frequently. Diagnosis is made by finding a convincing rhabdomyoblast, which may be extremely difficult. Generally, these tumors exhibit extreme pleomorphism and marked anaplasia (pl. VII-A, B). The nuclei are often large and vesicular. Marked nuclear variation is common, but pyknotic nuclei are rare. Giant cells and abnormal mitoses are common. Loose myxoid areas, spindle-cell areas, and solid cellular areas are often found within the same tumor. Microscopic foci of necrosis and hemorrhage are often present. Areas of alveolar and embryonal rhabdomyosarcoma are common even in a so-called adult rhabdomyosarcoma (see Fascicle 1, Second Series, "Tumors of the Soft Tissues"). No pure alveolar or embryonal rhabdomyo-

sarcomas were found in this series. Even those tumors which were predominantly of juvenile type had foci of adult rhabdomyosarcoma; therefore, we have chosen to consider all forms of rhabdomyosarcoma together.

Tremendous variation in the microscopic appearance of rhabdomyosarcoma is one clue to its diagnosis; however, actual diagnosis depends on finding rhabdomyoblasts. Several forms of rhabdomyoblasts exist: (1) Strap-shaped cells with two or more nuclei in tandem; (2) racket-shaped cells with a single nucleus at the expanded end of the cell and a tapering cell body extending into a point; (3) rounded cells, one nucleus and abundant cytoplasm, or giant cells with several nuclei and abundant cytoplasm; or (4) "spider-web" cells with peripheral vacuoles. The cytoplasm of these cells is deeply eosinophilic and often granular. Cross-striations may be seen at high magnification, especially with phosphotungstic-acid-hematoxylin stains (fig. 89). Usually, cross-striations are identified by light microscopy in only 20 to 30 percent of these tumors, but when these same cells are examined by electron microscopy, contractile elements, characteristic of striated muscle, are found in 90 percent or more. To facilitate ultrastructural study, the questionable rhabdomyoblasts are located first by light microscopy, then the appropriate area of the paraffin block is excised and processed for electron microscopy. Using this technic, in combination with light microscopy and special stains, we were able to identify cross-striations in each of the 26 tumors in this series.

Ultrastructurally (fig. 90), both thick and thin filaments (actin and myosin) and Z band material must be identified. Only rarely will these elements be organized into the characteristic sarcomere of striated muscle. Usually, fragments of Z band material and associated thick and thin filaments are haphazardly arranged throughout the cytoplasm. Occasional irregular masses of Z band material are present against the cell membrane, and disorganized thick and thin filaments fill the cytoplasm. Cell junctions are uncommon, but, occasionally, junctions with components of the intercalated disk (nexus, desmosome, and undifferentiated regions) are identified.

Immunofluorescent staining with anti-skeletal muscle antibodies has been used as

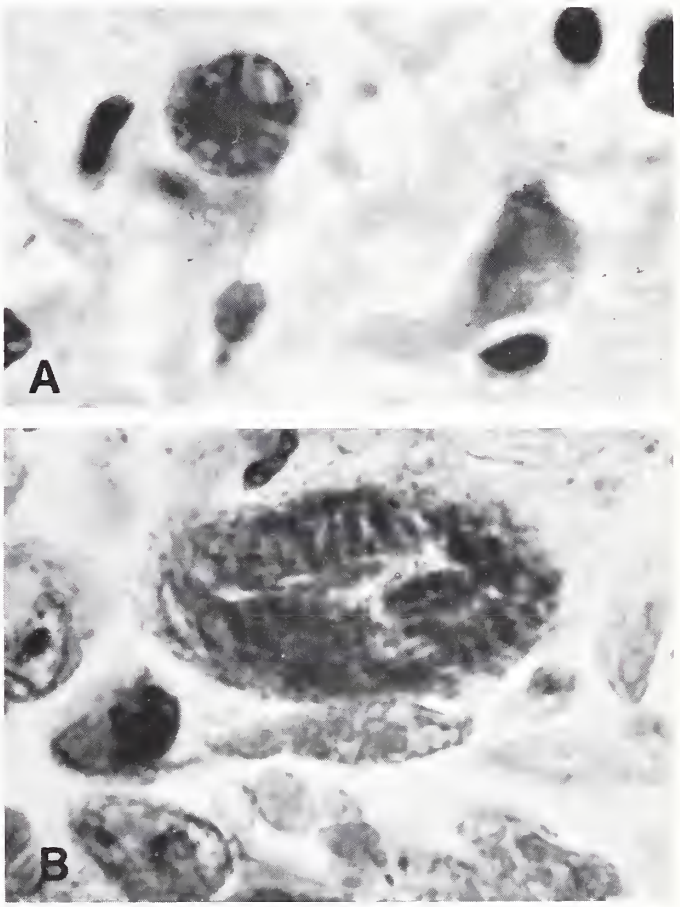


Figure 89
RHABDOMYOSARCOMA

With special stains and under oil immersion, cross-striations can be identified in every rhabdomyosarcoma; such striations, however, are not always 100 percent convincing. Phosphotungstic acid hematoxylin stain, (A) X1130; (B) X1405.

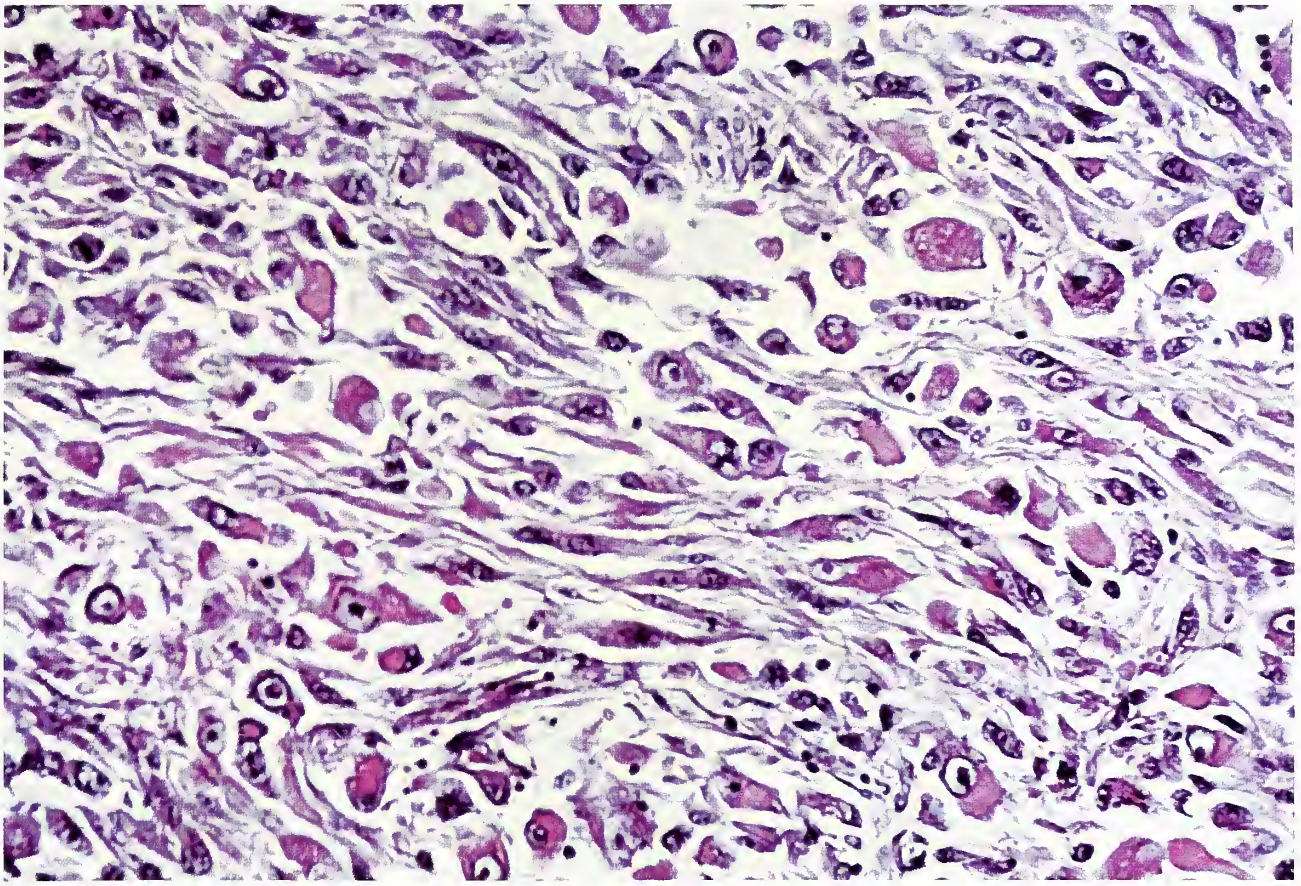
PLATE VII

RHABDOMYOSARCOMA
(Plate VII-A and B from same case)

A. Extreme cellular pleomorphism and nuclear atypia are characteristic of rhabdomyosarcoma. Multinucleated cells and abnormal, often bizarre, mitotic figures are frequent. Strap-shaped and racquet-shaped cells, the hallmark of rhabdomyosarcomas, are highly suggestive but not diagnostic of this entity. X195.

B. Racquet and strap cells of rhabdomyosarcoma have an eosinophilic, granular cytoplasm, with a frequent suggestion of cross-striations. Actual cross-striations are difficult to demonstrate, but are the only convincing way to establish the diagnosis. X530.

PLATE VII



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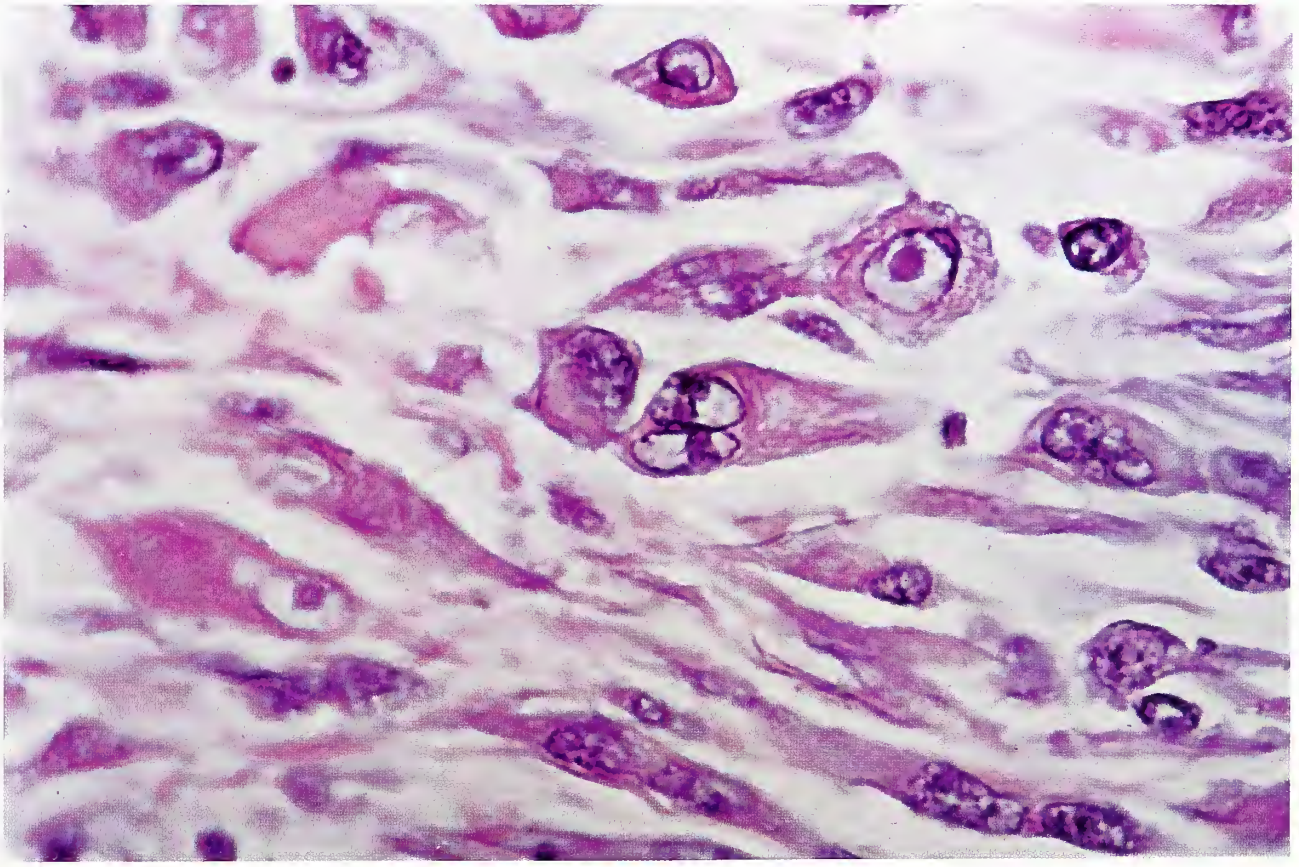

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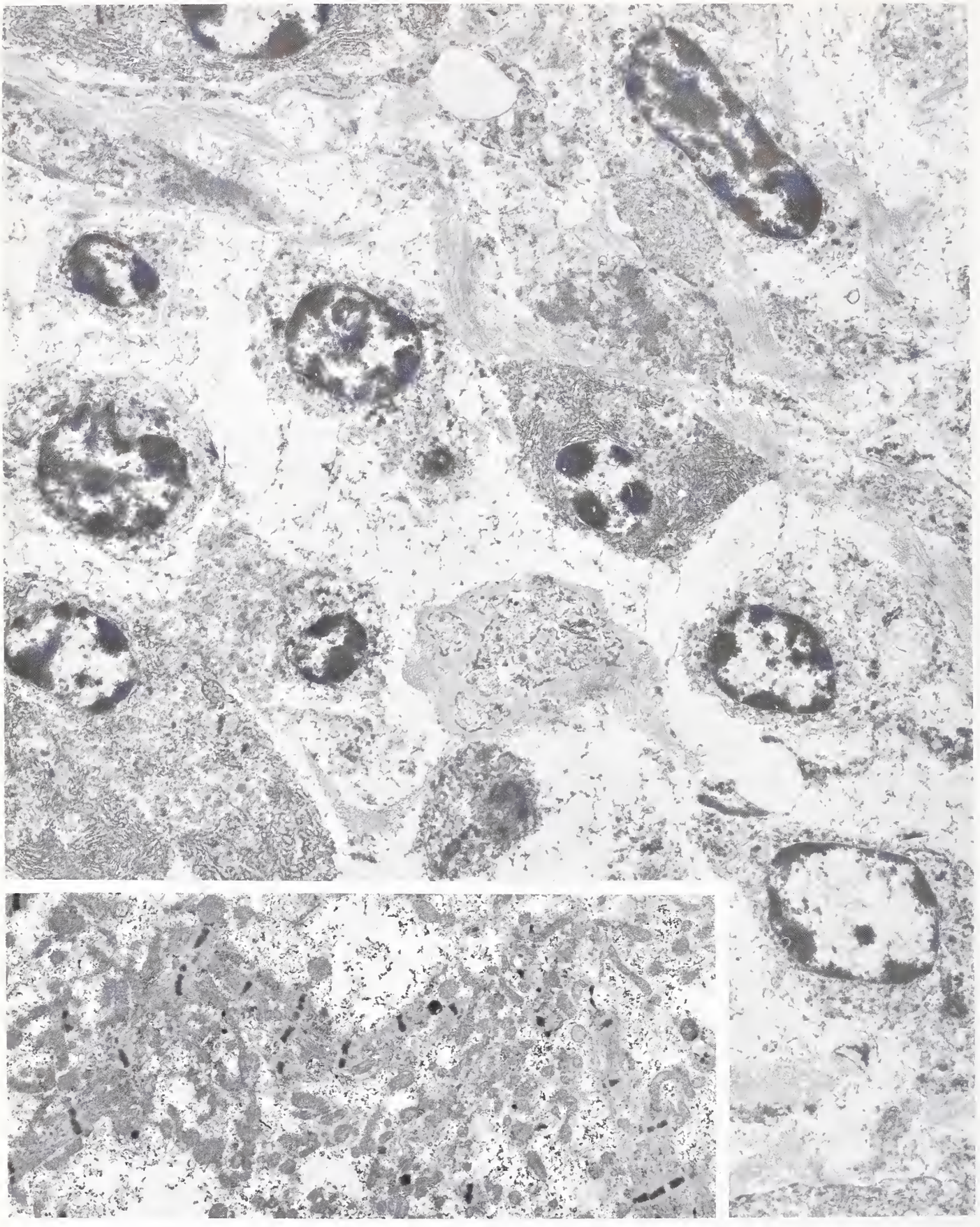

Figure 90
RHABDOMYOSARCOMA

Rhabdomyosarcoma consists of irregular cells with indistinct cell borders and atypical nuclei. The cytoplasm of these cells is filled with fibrils and abundant endoplasmic reticulum. Small densities may be discerned in many of these cells, often in apparent association with bundles of fibrils. Uranyl acetate and lead citrate, X5775.

Insert: At higher magnification, these densities are Z band material, either isolated or in association with myofilaments forming well defined sarcomeres. The finding of sarcomeric units in the tumor cells confirms the diagnosis of rhabdomyosarcoma. Uranyl acetate and lead citrate, X13,980.

an aid in the identification of a rhabdomyosarcoma. Generally, results with this technic have been disappointing and to date offer no advantage over light microscopy and histochemical technics.

Treatment. Excision of the main tumor mass, followed by combined radiation therapy and chemotherapy, is recommended. In spite of therapy, prognosis is generally poor, although 3-year survivals following treatment have been reported. The majority of patients, however, die within one year of diagnosis.

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FIBROSARCOMA AND MALIGNANT FIBROUS HISTIOCYTOMA

SYNONYMS AND RELATED TERMS: Fibromyxosarcoma; malignant xanthofibroma; fibroxanthosarcoma.

Definition. Fibrosarcoma and malignant fibrous histiocytoma are malignant mesenchymal tumors that are primarily fibroblastic in their differentiation. Much effort has been devoted to differentiating fibrosarcomas from malignant fibrous histiocytomas in the soft tissues, but we have chosen to deal with these tumors together, because both are derived from fibroblasts and few examples primary in the heart are available for comparison of either entity.

Clinical Aspects. Clinical findings of the 14 patients in the AFIP series are summarized in Table 21. Five of the 14 patients had distant metastases involving other viscera; in two patients, direct spread of the tumor involved adjacent structures. The greatest tumor mass was in the heart in each patient in this series, and their ages ranged from less than one year to 87 years.

Clinical findings associated with these tumors are often multiple and confusing. Important findings in patients with fibrosarcoma of the heart include systolic murmurs, often of changing intensity and recent onset; nonspecific electrocardiographic changes, including S-T segment and T wave changes, low voltage, and bundle branch block; arrhythmias, especially atrial arrhythmias; and findings of pericardial disease, including pleuritic chest pain, fever, and dyspnea. Eighty percent of the patients in this series had one or more of these symptoms. In addition, two patients

TABLE 21

MALIGNANT CARDIAC FIBROBLASTIC TUMOR CLINICAL FINDINGS IN 14 PATIENTS

Findings	Number of Patients
Cardiac murmurs	7
Pleuritic chest pain, fever, dyspnea	6
Nonspecific electrocardiographic changes	5
Congestive heart failure	4
Cyanosis	2
Dyspnea	2
Embolic phenomena	2
Weight loss, fever, malaise	2
Anginal chest pain	1

TABLE 22

MALIGNANT CARDIAC FIBROBLASTIC TUMOR
LOCATION OF TUMOR IN 14 PATIENTS

	Number of Patients	Primary Site*
Right ventricle	8	4
Left ventricle	6	2
Right atrium	6	2
Left atrium	5	4
Pericardium	5	

*Primary site could not be determined for 2 patients.

had symptoms usually suggestive of malignancy—weight loss, fever, and malaise.

Description. These tumors may be nodular or infiltrative, but are always firm and white or gray-white (fig. 91). They arise with equal frequency on the left and right sides of the heart (Table 22). There was no predilection of these tumors for any single site in the heart. In nine patients, the tumor involved multiple sites within the heart. In five patients, the pericardium was invaded, often both the visceral and parietal layers. No fibrosarcoma primary in the pericardium was found in the AFIP collection. A portion of the tumor was intracavitary in 50 percent of patients; there was significant obstruction of a valve orifice or invasion of a valve leaflet in each patient. The mitral valve was involved in four patients; the pulmonary valve in two; and the tricuspid valve in one.

Microscopically, fibrosarcomas consist of spindle-shaped cells, with elongated but blunt-ended nuclei, and tapering cytoplasm (fig. 92). Usually, nucleoli are not apparent. Pleomorphism and anaplasia are generally minimal; however, mitoses are frequent. Spindle cells are arranged haphazardly or in broad bundles or fascicles, which often course at acute angles to one another. Palisading nuclei and interlacing cords of cells are not features of fibrosarcoma. Regularly arranged bundles of spindle cells in the fibrosarcoma are associated with a parallel arrangement of collagen and reticulin fibers, best appreciated with trichrome and reticulum stains. Foci of myxoid change are frequently encountered; however, actual tumor necrosis is rare. Islands of adult differentiated cartilage and bone are often present, but do not provide sufficient evidence for classifying these tumors as malignant mesenchymomas (fig. 93). By definition, a malignant mesenchymoma is composed of two or more unrelated, malignant, mesenchymal forms, usually exclusive of any fibrosarcomatous area.

Malignant fibrous histiocytoma has fibrosarcomatous areas, often identical to differentiated fibrosarcoma (fig. 94). A storiform or whorled pattern of the spindle cells and the presence of giant cells differentiate malignant fibrous histiocytoma

from fibrosarcoma. These features were present in five patients in this series. Criteria for establishing the malignancy of these tumors are anaplasia and mitoses; however, the only positive means of making the correct diagnosis are distant metastases or multiple sites of involvement within the heart.

Ultrastructurally, both fibrosarcoma and malignant fibrous histiocytoma consist primarily of fibroblastic cells. The nuclei are usually multilobed, and the cell body is elongated with multiple cytoplasmic processes. The cells lack a basement membrane, and collagen fibrils and tropocollagen are present in cellular bays, closely associated with the cell membrane. The cytoplasm contains abundant rough-surfaced endoplasmic reticulum, Golgi vesicles, annulate lamellae, and dilated cisterni. Mitochondria are infrequent and often of abnormal configuration. Many of the cells contain abundant cytoplasmic filaments, often arranged in bundles near the nuclei. Cell junctions are rare. In addition, malignant fibrous histiocytomas contain so-called pale cells. These cells are ovoid with few cytoplasmic processes, and sparse rough-surfaced endoplasmic reticulum.

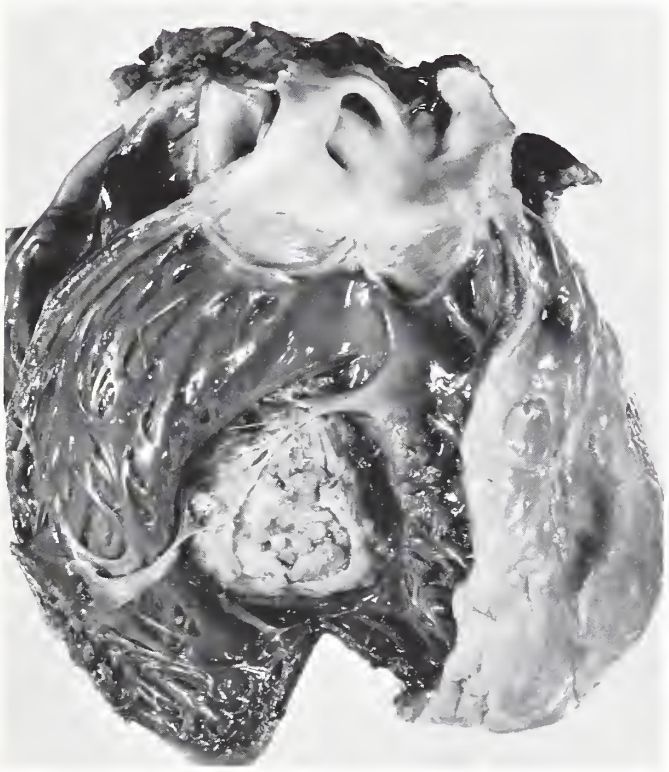

Figure 91
FIBROSARCOMA

This large fibrosarcoma arose in the ventricular septum and protruded into the right ventricle. Unlike fibromas, their benign counterparts, fibrosarcomas arise with near equal frequency in all cardiac chambers. They do not occur most frequently in the ventricular septum. Multiple sites of cardiac involvement are common in patients with fibrosarcomas.

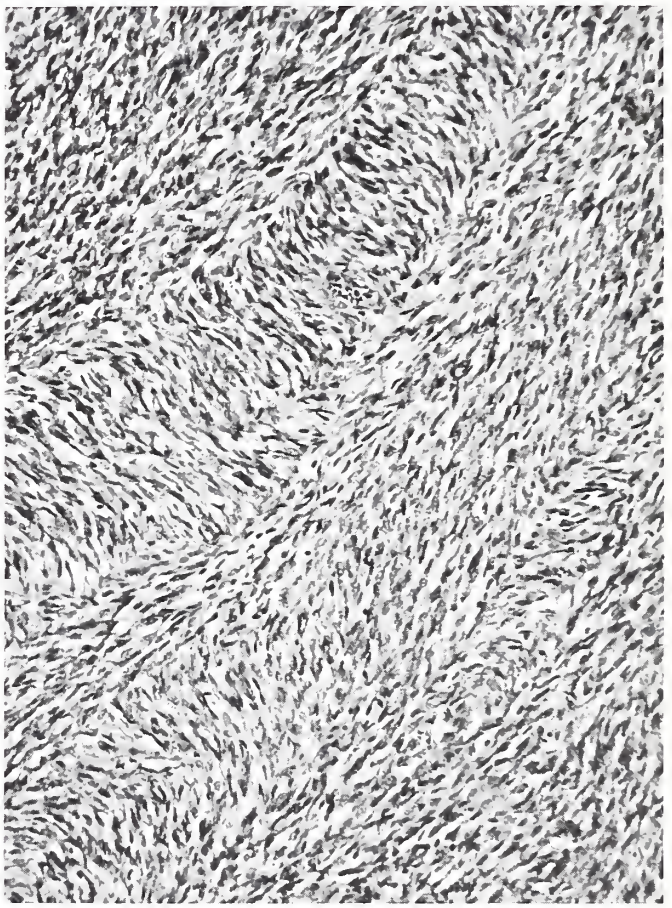

Figure 92
FIBROSARCOMA

A fibrosarcoma is composed of spindle-shaped cells arranged in broad fascicles, which frequently course at acute angles to one another. Nuclear atypia and cellular pleomorphism may be prominent. Distant metastases or multiple sites of involvement within the heart are the only true criteria of malignant tumors. X14.

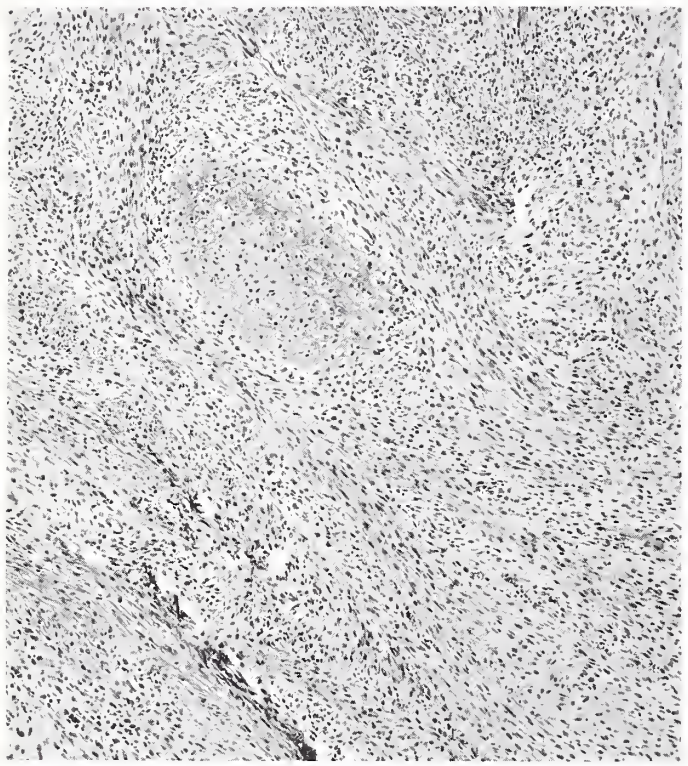

Figure 93
FIBROSARCOMA
Foci of metaplastic cartilage and bone appear frequently in fibrosarcomas, but are not sufficient evidence to classify a fibrosarcoma as a malignant mesenchymoma. X50.

Like fibroblastic cells, however, they lack a basement membrane.

Treatment. The tumor was diagnosed with the aid of angiography in three patients in this series, and surgery was attempted. Surgical excision was not feasible and each patient died postoperatively. No therapy has been effective for treatment of malignant fibroblastic tumors of the heart, although radiation and chemotherapy have been tried with minimal success. Prognosis is poor; all patients in the AFIP series died within two years of onset of symptoms.

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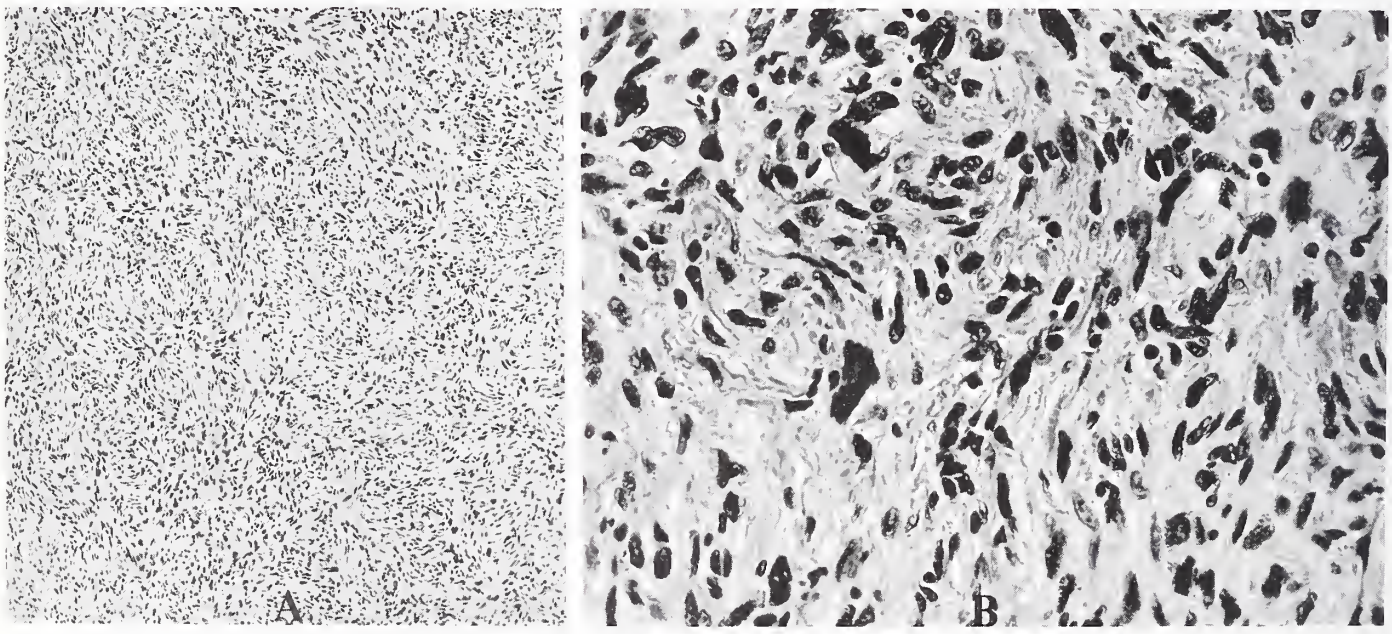

Figure 94
FIBROSARCOMA
A number of fibrosarcomas in the AFIP study should probably be more correctly classified as malignant fibrous histiocytomas. These tumors have a whorled or storiform appearance (A) and contain large, often multinucleated, histiocytic cells (B) in addition to spindle-shaped fibroblasts. (A) X50; (B) X300.

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MALIGNANT LYMPHOMA

SYNONYMS AND RELATED TERMS: Reticulum cell sarcoma; lymphosarcoma; Hodgkin's disease.

Definition. An extranodal malignant lymphoma is a malignant lymphoma of any cell type primarily involving an organ other than the lymph nodes, thymus, liver, spleen, bone marrow, or Waldeyer's ring, without evidence of dissemination beyond the primary site. A primary lymphoma of the heart must involve **only** the heart and pericardium. The histologic classification of lymphoma is covered in detail in "Tumors of the Hematopoietic System," Fascicle 8, First Series, and will not be discussed in this fascicle.

Clinical Aspects. Seven primary malignant lymphomas of the heart are included in the AFIP series. Patients ranged in age from 18 to 77 years, with a nearly equal incidence among men and women. Malignant lymphomas primary in the heart have been found in patients from 14 months to 84 years of age.

Lymphoma was an incidental finding at necropsy in three patients in this series; in the remaining four patients, congestive heart failure, cardiomegaly, and pericardial effusion were the most common findings. All four patients died of intractable congestive heart failure, without clinical suspicion of malignant disease.

Description. All sites in the heart were involved, without apparent predilection for any specific site. In two patients, lymphoma involved the pericardium, both visceral and parietal, and the myocardium diffusely (fig. 95). Both patients had cardiomegaly by chest roentgenogram and died of intractable congestive heart failure. In the remaining five patients, the lymphoma was localized (fig. 96), although there were multiple sites of involvement in three patients (Table 23). A portion of the

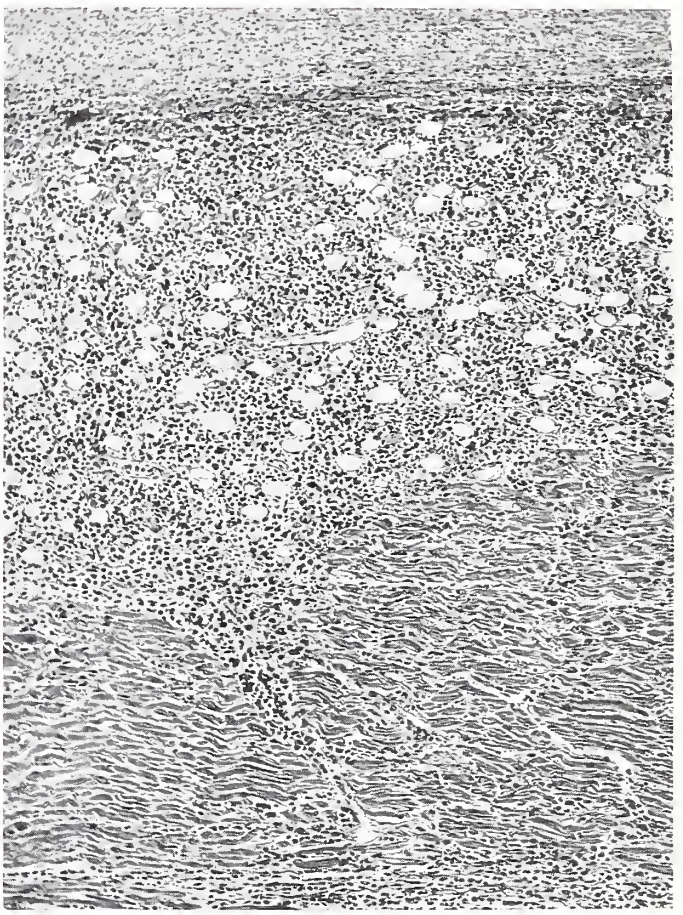

Figure 95
MALIGNANT LYMPHOMA
The heart is occasionally the primary site of an extranodal malignant lymphoma. Diffuse lymphomas, as illustrated here, often involve both layers of the pericardium as well as the myocardium. To be classified as a primary cardiac lymphoma, however, the lymphoma must be confined to the heart, without evidence of involvement of other tissues or contiguous structures. X100.

TABLE 23

CARDIAC MALIGNANT LYMPHOMA
LOCATION IN 5 PATIENTS*

Site	Number of Patients
Left atrium	3
Left ventricle	3
Right ventricle	2
Right atrium	2
Pericardium	2

*Excluding 2 patients with widespread diffuse involvement of the pericardium and myocardium.

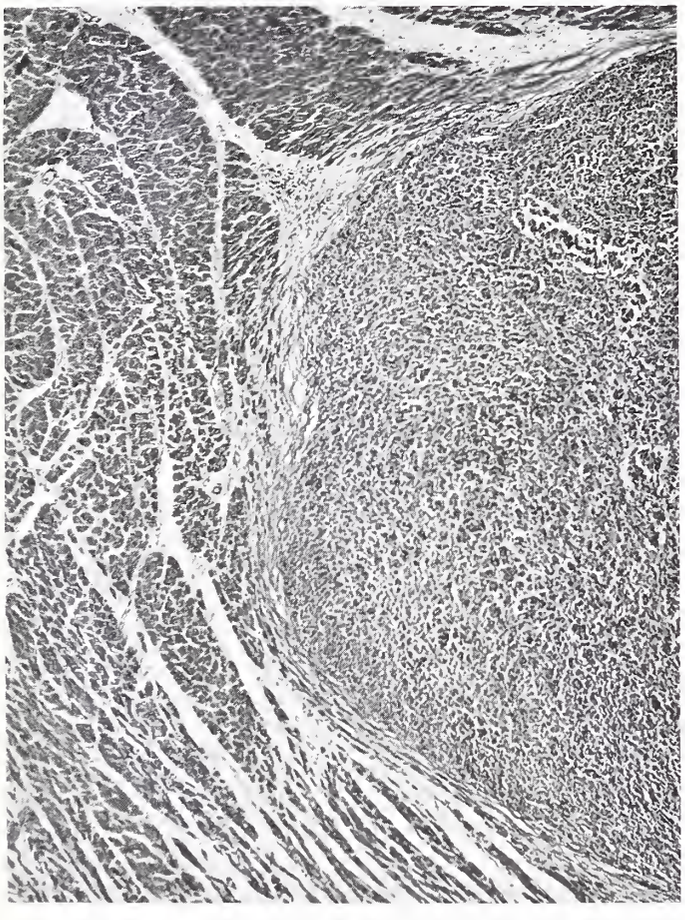

Figure 96
MALIGNANT LYMPHOMA

Focal, apparently circumscribed collections of malignant lymphoma cells are more frequent than diffuse lymphomas. Often, localized primary cardiac lymphomas are poorly differentiated and there are multiple sites of involvement within the heart. X50.

lymphoma was intracavitary in two patients, and partially obstructed the pulmonary valve in another.

Treatment. Surgical excision, followed by radiation therapy, is the treatment of choice for extranodal malignant lymphoma. Remission of symptoms following radiation therapy has been reported in a patient with primary malignant lymphoma of the heart. In none of the patients in this series was the tumor diagnosed antemortem; all patients died within a year of onset of symptoms.

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EXTRASKELETAL OSTEOSARCOMA

SYNONYMS AND RELATED TERMS: Extraskeletal osteogenic sarcoma; extraosseous osteogenic sarcoma; osteoblastic sarcoma; osteoid sarcoma.

Definition. Osteosarcomas are tumors composed in part, or entirely of osteoid in continuity with a sarcomatous stroma. Extraskeletal variants are identical morphologically to those involving bone; however, they involve sites exclusive of the skeletal system. In the five extraskeletal osteosarcomas of the heart in the AFIP collection, the largest tumor mass was present in the heart and metastases did not involve the skeletal system.

Clinical Aspects. Findings in the five patients in our series, similar to those of other sarcomas of the heart, were progressive congestive heart failure or dyspnea and cardiac murmurs of recent onset. Systolic murmurs were present in three of the patients; in all three, an intracavitary tumor was diagnosed with the aid of angiography, and the intracavitary portion of the tumor was excised surgically. The patients, four of whom were men, ranged in age from 16 to 58 years.

Description. Of the five tumors, three were primary in the left atrium (fig. 97), one in the right atrium, and one in the right ventricle. A portion of the tumor was intracavitary in four patients; the mitral valve was obstructed in two, the tricuspid valve in one, and the pulmonary valve in one. In the fifth patient, both the mitral and aortic valves were invaded by the tumor, although neither valve orifice was obstructed.

Microscopically, the tumors consisted, at least in part, of osteoid (fig. 98) in association with sarcomatous cells. Multinuclear giant cells and pleomorphic round cells often surrounded the foci of osteoid. The round cells had varying amounts of eosinophilic cytoplasm, hyperchromatic and irregular nuclei, and irregular cell borders. There was a granular intracellular

Figure 97
OSTEOSARCOMA
(Figures 97 and 98 from same case)
This osteosarcoma arose in the left atrium. A large portion of the osteosarcoma is intracavitary and has partially replaced the mitral valve, obstructing the valve orifice.

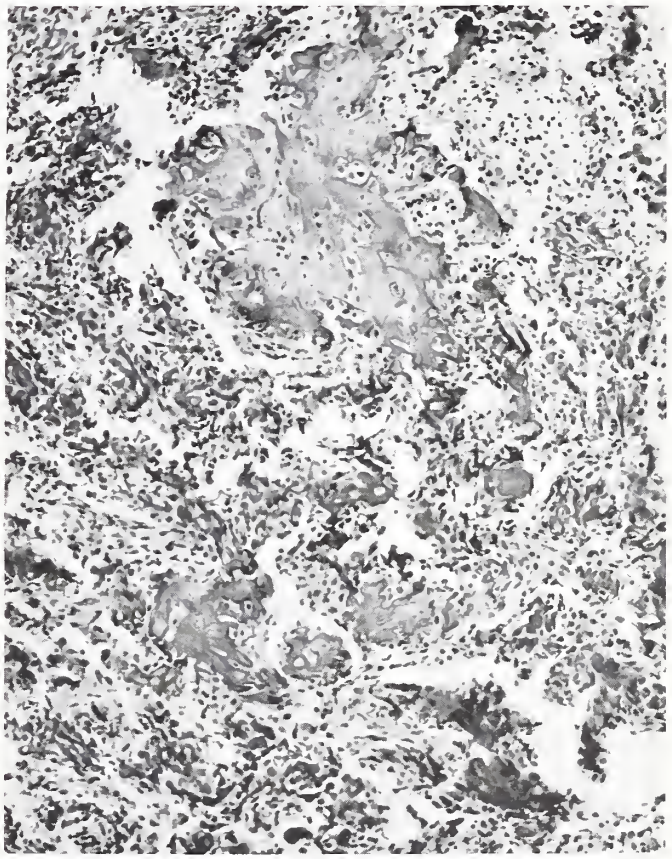

Figure 98
OSTEOSARCOMA
In the same tumor shown in figure 97, foci of osteoid and malignant osteoblasts are characteristic of extraskeletal osteosarcoma. The osteoid is surrounded by pleomorphic round cells and spindle cells, and foci of cartilage with malignant chondroblasts are frequently present. The large round cells stain positively with alkaline phosphatase stains. X80.

accumulation of diastase-digestible, periodic acid-Schiff positive polysaccharide in the round cells. In addition, these cells stain positively with alkaline phosphatase stains. All the tumors in this series had fibrosarcomatous areas, often in close association with areas of osteoid and malignant osteoblasts; in two tumors, there were foci of apparent chondrosarcoma.

In three patients, metastases were to the lungs, adjacent soft tissues, or liver. Metastases and secondary sites of involvement within the heart contained foci of osteoid and were composed entirely of osteoid and malignant osteoblasts in two tumors.

Many tumors, especially fibrosarcomas, contain foci of metaplastic bone and/or cartilage; they must not be confused with extraskeletal osteosarcomas. Metaplastic bone is normally differentiated adult bone; although the osteoblasts and osteoclasts associated with this bone are large, they are regular, with minimal pleomorphism and anaplasia. Metaplastic bone should not be confused with the osteoid of osteosarcoma. Of further aid is the fact that sarcomas with foci of metaplastic bone and cartilage rarely exhibit the same metaplasia in the metastases, while metastases of extraskeletal osteosarcoma are composed, at least in part, of malignant osteoblasts in association with osteoid.

Treatment. One patient, who lived four years after onset of symptoms, was treated with radiation therapy and chemotherapy, following excision of the intracavitary portion of the tumor. The remaining four patients in the series died within two years, in spite of surgery, radiation therapy, and/or chemotherapy.

Extraskeletal Chondrosarcoma

At least two extraskeletal osteosarcomas in this series contained foci of chondrosarcoma. No examples of pure **extraskeletal chondrosarcoma** nor of mesenchymal chondrosarcoma primary in the heart were found in the AFIP collection. Such tumors, however, have been reported.

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MALIGNANT NERVE SHEATH TUMORS

SYNONYMS AND RELATED TERMS: Malignant schwannoma; neurofibrosarcoma; malignant neurinoma; neurogenic sarcoma; nerve sheath fibrosarcoma; malignant neurilemoma.

Definition. This category is reserved for those tumors that demonstrate distinctive morphologic characteristics of Schwann cell differentiation or originate within the perineurium of sizable nerves. These tumors presumably are derived from the cells of nerve sheaths.

Clinical Aspects. All four patients in the AFIP series were male, ranged in age from 9 to 52 years, and presented with pleuritic chest pain, dyspnea, and pericardial effusion. Two patients had nonspecific electrocardiographic findings—low voltage and left ventricular strain. A systolic murmur was present in one patient. In three of our patients the diagnosis of pericardial tumor was made antemortem, with the aid of angiocardiography and echocardiography. Surgical excision was attempted in each patient.

Description. All four tumors involved the visceral pericardium over the base of the heart. In three patients, primary involvement was over the outflow of the right ventricle and pulmonary artery; in the fourth patient, the bulk of the tumor was situated over the right atrium. In each patient, the underlying myocardium was invaded; in two, the parietal pericardium was involved. The bulk of the tumor mass was intrapericardial in all four patients. In one, the adjacent mediastinum was involved, and there were metastases to the lungs in two patients.

Microscopically, these tumors are composed of plump spindle cells, with ovoid rather than elongated nuclei. The spindle cells are arranged in wavy fascicles that resemble Schwann cell cords, or in interlacing bundles, often in a herringbone pattern (fig. 99). Nuclei are in parallel arrangement, and microscopic foci of necrosis, bordered by cells arranged in palisades, are numerous (fig. 100). Mitoses are frequent, as is a moderate degree of pleomorphism and nuclear atypia.

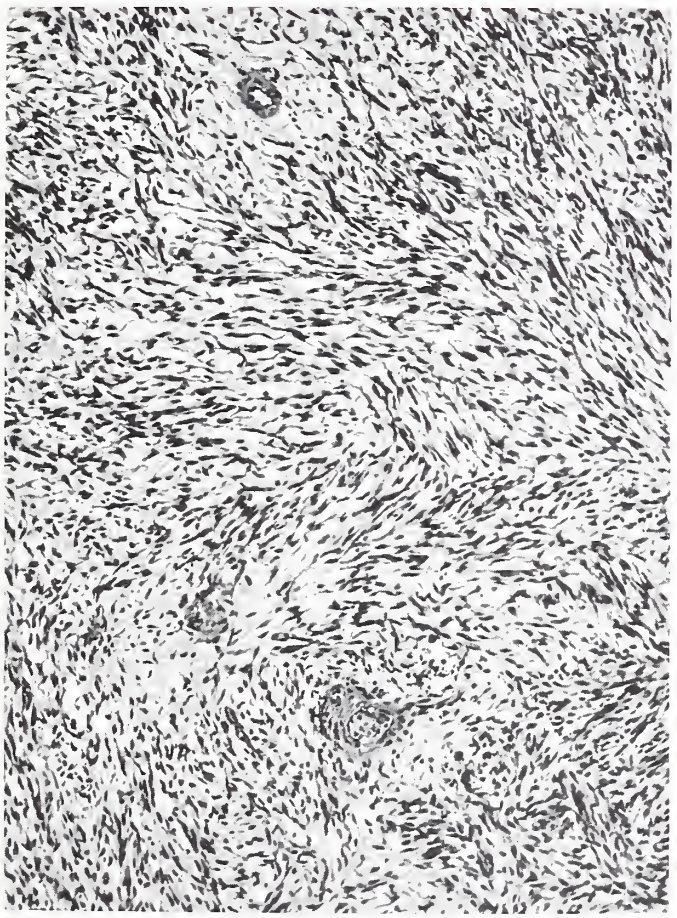

Figure 99
MALIGNANT NERVE SHEATH TUMOR
This malignant nerve sheath tumor is composed of slender spindle cells arranged in whorls and interlacing fascicles. The nuclei appear to be in parallel arrangement, and bundles of spindle cells are interspersed in a myxoid finely fibrillar matrix. This cellular pattern is reminiscent of Antoni types A and B areas seen in benign schwannoma. X90.

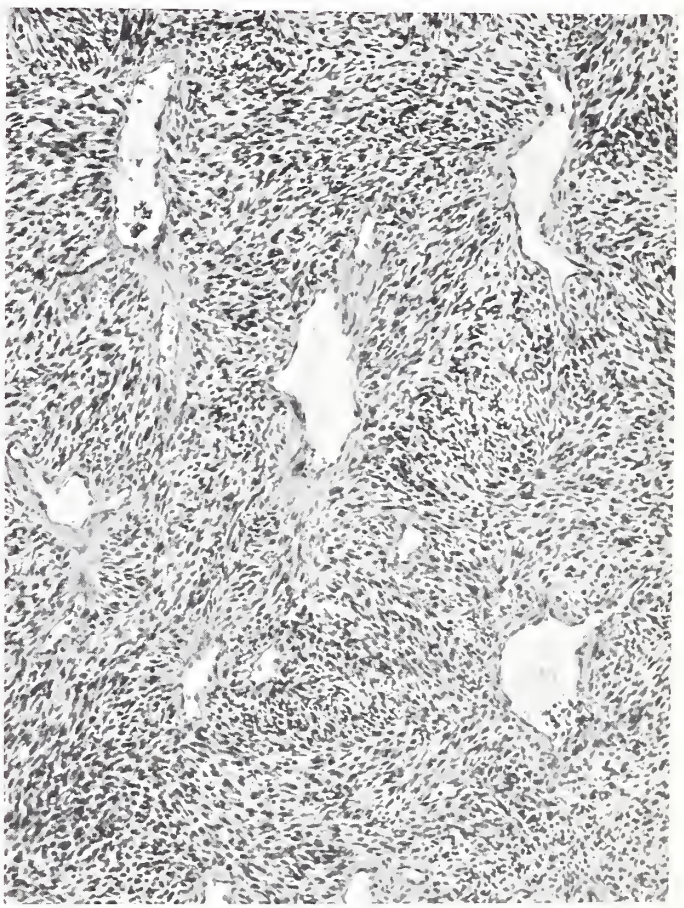

Figure 100
MALIGNANT NERVE SHEATH TUMOR
Other areas in malignant nerve sheath tumors have a distinctly organoid pattern. Nuclear palisading around areas of necrosis or surrounding vascular channels, as shown here, is a characteristic feature of malignant tumors of peripheral nerves. X70.

Ultrastructurally, these cells resemble fibroblasts with multilobed nuclei, numerous cytoplasmic processes, and abundant rough endoplasmic reticulum. Unlike fibroblasts, however, malignant Schwann cells have an extensive and well developed basement membrane surrounding each cell. This feature clearly distinguishes Schwann cells from fibroblasts. Many malignant Schwann cell tumors also contain abundant fibrous long-spacing collagen. This was once thought to be pathognomonic of nerve sheath tumors; however, fibrous long-spacing collagen has been reported in many other tumors, as well as in the normal heart.

It has been theorized that malignant nerve sheath tumors of the heart originate in the cardiac plexus or the vagus nerve innervation of the heart. At the time of necropsy, the tumors were too large to verify this theory. However, all reported malignant nerve sheath tumors, as well as the four tumors in this series, were located on the visceral pericardium at the base of the heart on the right side—the exact location of the vagus nerve innervation of the heart.

Treatment. In spite of radiation and chemotherapy following surgical excision of the main intrapericardial tumor mass, 2 of the 3 patients who were diagnosed antemortem died within a year. The third patient had evidence of recurrent disease one year following surgery.

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MALIGNANT TERATOMA

SYNONYMS AND RELATED TERMS: Teratocarcinoma.

Definition. A malignant teratoma is a teratoma in which one of the elements has undergone a malignant change, either metastasizing to or invading adjacent structures. The malignant portion may be a carcinoma or a sarcoma. When the malignant portion of the tumor is embryonal

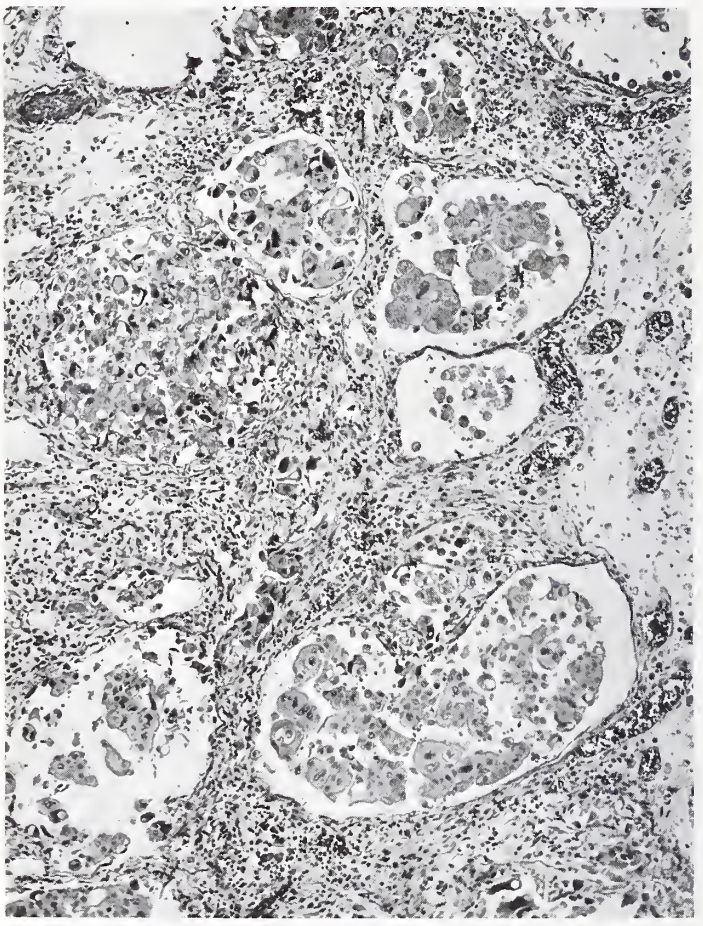

Figure 101
MALIGNANT TERATOMA
(Figures 101 and 102 from same case)
The malignant portion of a cardiac teratoma is most frequently embryonal carcinoma. The large polygonal epithelial cells often fill or line acinar structures, although tubular and papillary forms are also common. X90.

carcinoma, the tumor is termed teratocarcinoma.

Clinical Aspects. All four malignant teratomas in the AFIP collection occurred in children—three girls and one boy, ranging in age from 1 to 4 years. Each child in this series had congestive heart failure, usually associated with anorexia and vomiting. All four patients had cardiomegaly by chest roentgenogram—two had arrhythmias and nonspecific electrocardiographic findings and one had a systolic murmur.

Surgical excision of the pericardial mass was attempted in one patient; however, the tumor had invaded the heart so extensively that excision was impossible. All four children died within three months of onset of symptoms.

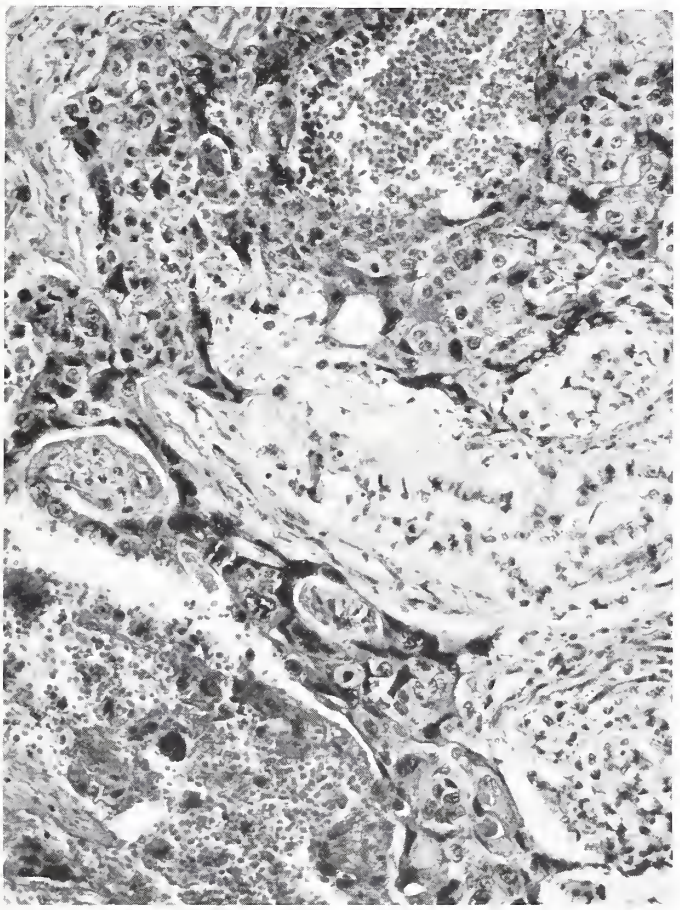

Figure 102
MALIGNANT TERATOMA

Foci of choriocarcinoma, characterized by clusters of cytotrophoblasts, uniform cells with clear cytoplasm surrounded by syncytiotrophoblasts, and elongated cells with deeply eosinophilic cytoplasm, are often present in the malignant teratoma in association with embryonal carcinoma (same tumor as shown in figure 101). Such tumors should not be diagnosed solely as choriocarcinoma. X140.

Description. Three of the tumors were primarily intrapericardial, attached to the root of the aorta and pulmonary artery; in each, elements derived from all three germ layers were identified. Two patients had metastases to lungs and mediastinum, and there was extensive invasion of the myocardium of the left and right ventricles in another patient. The malignant portion of the teratoma was identified as embryonal carcinoma in two patients and as squamous cell carcinoma in a third. In the fourth patient, the tumor was situated over the anterior surface of the heart and had invaded the ventricular septum and right ventricle. A large portion of the tumor was intracavitary within the right ventricle, but did not appear to obstruct either the tricuspid or pulmonic valve. The bulk of this tumor and the pulmonary metastases were both embryonal carcinoma (fig. 101) and choriocarcinoma (fig. 102). Remnants of cystic structures were found on the anterior aspect of the heart. These structures were lined by ciliated columnar and squamous epithelium, containing islands of cartilage within the cyst wall. Although derivatives of all three germ layers were not found in this tumor, the most likely diagnosis was embryonal carcinoma arising in a teratoma.

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THYMOMA

Thymomas are primarily tumors of the anterior mediastinum, derived from the thymus gland. Occasionally, however, a thymoma is primary within the pericardium, derived from thymic rests which are not infrequently encountered in the normal parietal pericardium. Only tumors in which there is no evidence of anterior mediastinal involvement are acceptable as primary pericardial thymomas. The histology of thymomas is reviewed in "Tumors of the Thymus," Fascicle 13 of the Second Series, and will not be discussed in this fascicle.

There are four thymomas originating in the parietal pericardium in the AFIP series. Three of the 4 adults were women. In one patient, thymoma was an unexpected finding at autopsy. The remaining three patients had clinical findings of intractable congestive heart failure, pericardial effusion, and a mediastinal or pericardial mass by chest roentgenogram. At operation, each patient had an intrapericardial thymoma attached to the pericardium, either at the base of the heart or anterior to the heart. There was no evidence of myasthenia gravis in any patient in this series.

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OTHER MALIGNANT CARDIAC TUMORS

LEIOMYOSARCOMA

Malignant tumors derived from smooth muscle are extremely rare in the heart and pericardium. Only one such tumor is in the AFIP collection. The patient was a 27 year old man who developed atrial fibrillation, accompanied by pleuritic chest pain, fever, and syncopal episodes. An intracavitary mass was demonstrated by angiography in the left atrium, and surgical excision was attempted. The tumor arose in the left atrium, invaded the myocardium, and partially filled the left atrial cavity. No metastases were found at necropsy.

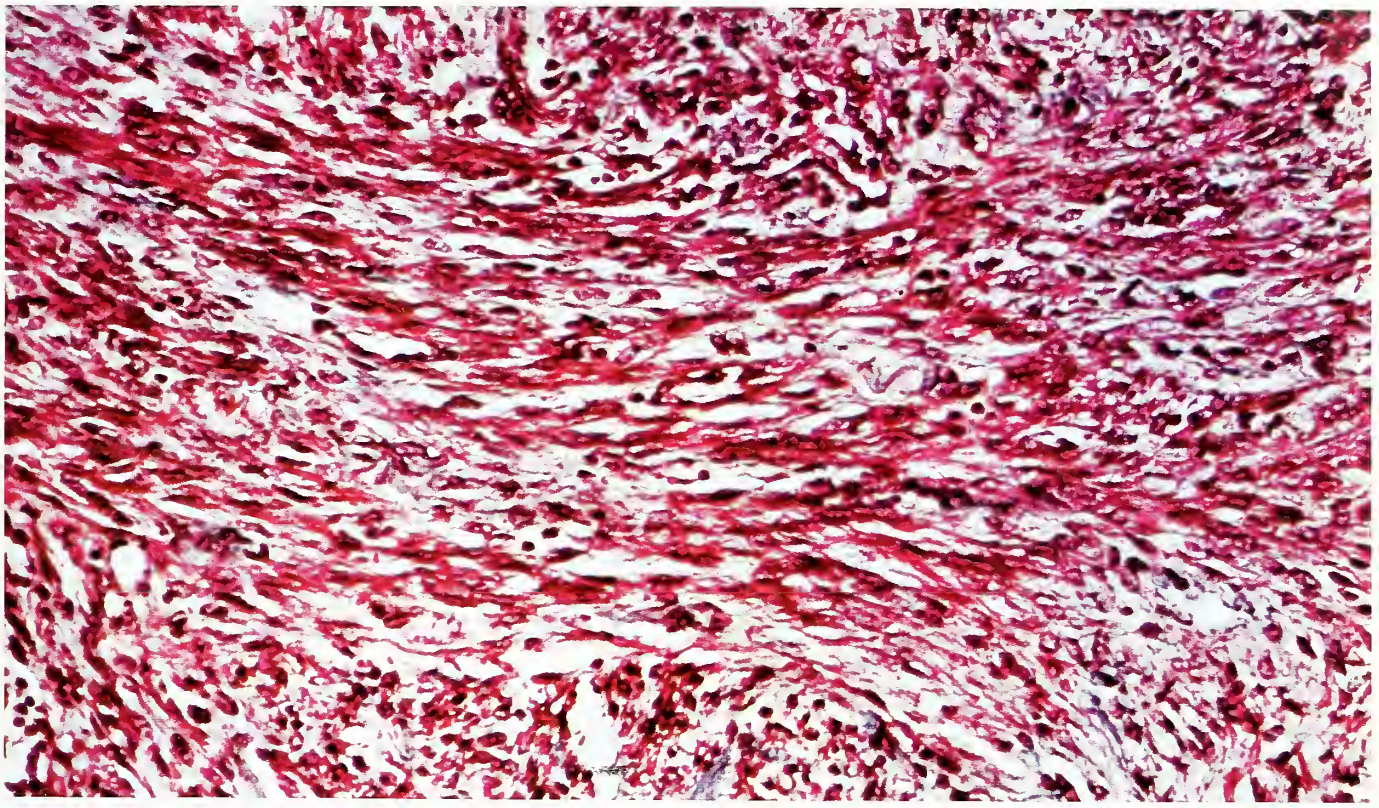
Microscopically, leiomyosarcomas in the heart, as well as leiomyosarcomas of soft tissues, are recognized by their elongated cells with blunt-ended nuclei. These cells grow in interlacing cords, and the suggestion of nuclear palisading is often present. The cytoplasm is eosinophilic and stains red-purple with Masson's trichrome stain, often with the distinct impression of abundant myofibrils lacking cross-striations (pl. VIII-A). The nuclei may be large and vesicular or hyperchromatic, and mitoses are often, but not always numerous.

Ultrastructurally, these cells contain haphazardly oriented bundles of myofibrils with characteristic spindle-shaped densities, presumably tropomyosin. The cell membrane is distinct and there is a well defined basement membrane. Marginal dense bodies, similar to the spindle-shaped densities of the myofibrils, are frequently found against the cell membrane. These ultrastructural features distinguish leiomyosarcomas from fibrosarcomas and neurogenic sarcomas.

Approximately eight leiomyosarcomas of the heart have been reported; however, in at least half of the cases, the heart was not unequivocally the primary site of the tumor.

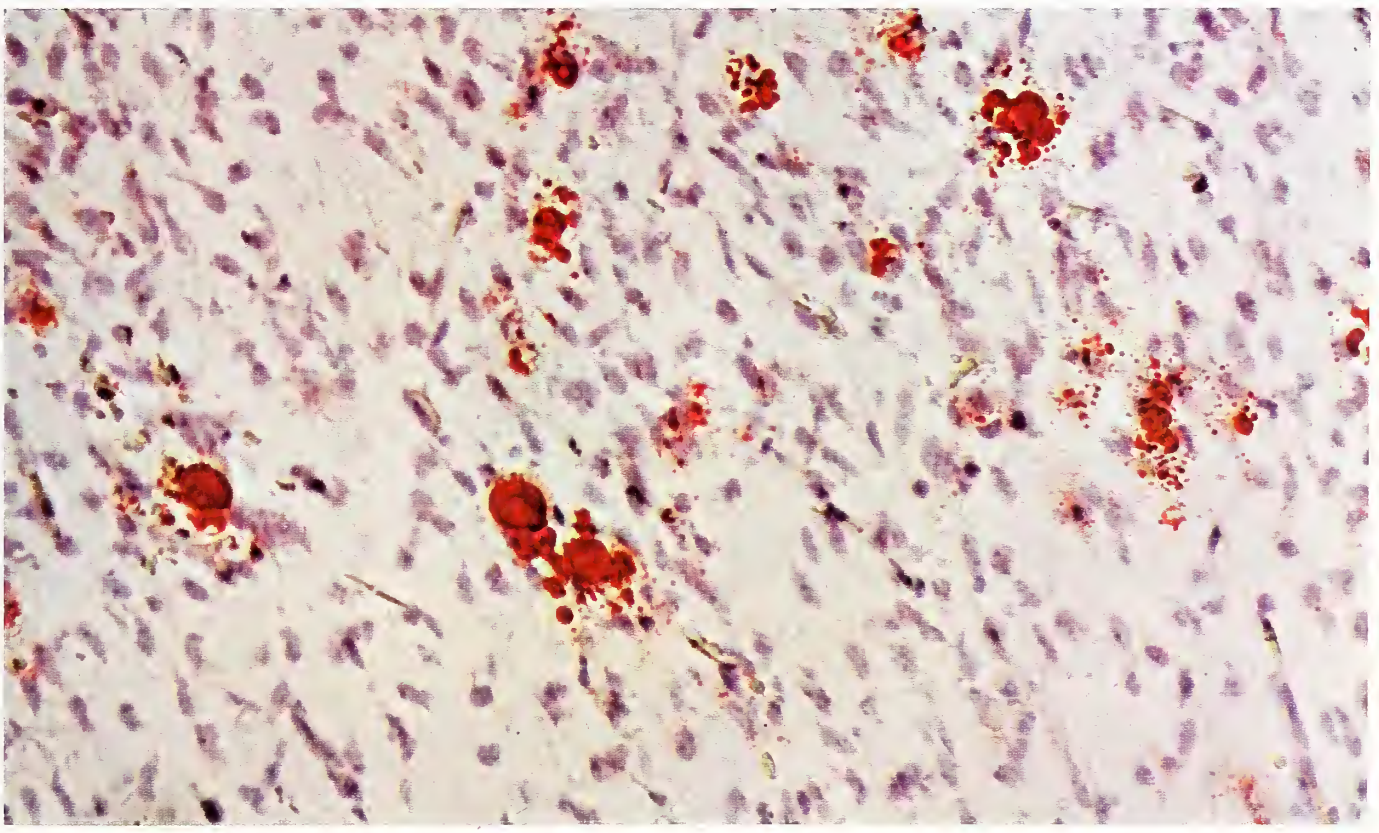
PLATE VIII

LEIOMYOSARCOMA



A. This leiomyosarcoma is composed of elongated cells with blunt-ended nuclei. With trichrome stains, the cytoplasm is distinctly acidophilic and granular; however, myofilaments are usually not discernible. Characteristically, intercellular collagen is scant or absent. Masson's trichrome stain, X195.

LIPOSARCOMA



B. Diagnosis of liposarcoma is confirmed by the presence of lipid laden cells with peripherally placed nuclei, even in spindle cell or myxoid areas of the tumor. Oil red O stain, X290.

LIPOSARCOMA

Although lipomas of the heart are relatively frequent, liposarcomas of the heart and pericardium are distinctly rare. There is only one such tumor in the AFIP collection; a 30 year old woman with severe congestive heart disease was thought to have chronic rheumatic heart disease. At necropsy, however, a large tumor replaced the right atrium and extended to the pericardium, constricting the superior and inferior vena cava. No metastases were found.

Microscopically, the tumor resembled embryonal adipose tissue; signet-ring cells and stellate cells with numerous tiny vacuoles were abundant, and myxoid areas were frequent (fig. 103). The vacuoles and intracellular spaces stained intensely with the oil red O stain, even on frozen sections from formalin-fixed tissue (pl. VIII-B).

Only six liposarcomas, primary in the heart or pericardium, have been reported in the literature.

SYNOVIAL SARCOMA

A 30 year old man was the only patient in the AFIP collection with a synovial sarcoma primary in the heart. He had progressive dyspnea, syncopal episodes, and a

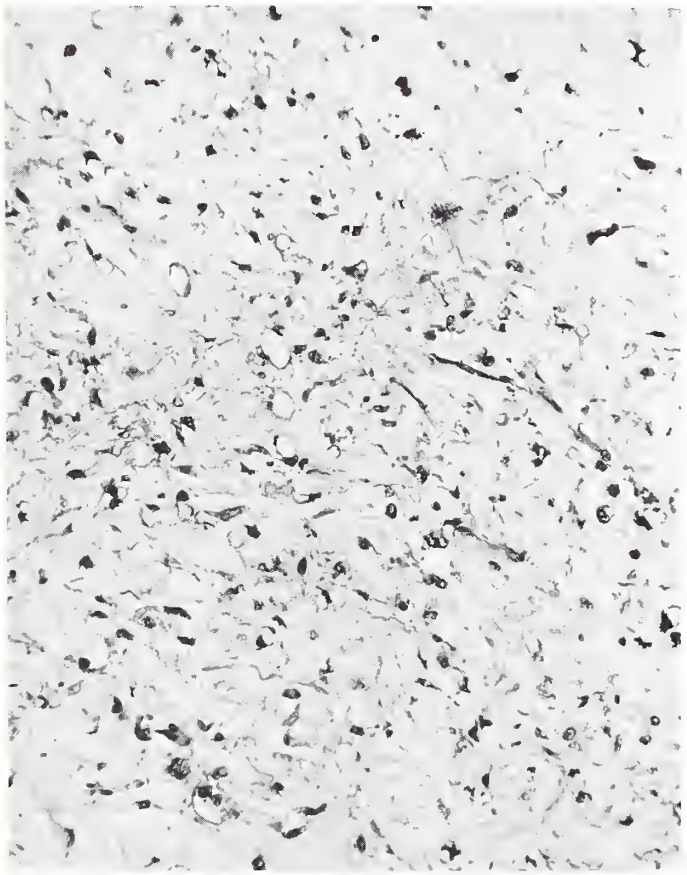


Figure 103
LIPOSARCOMA
Signet-ring cells which are lipoblasts are characteristic of the liposarcoma. Frequently, there are extensive myxoid areas in liposarcomas. Spindle cell foci, which resemble fibrosarcoma, may also be prominent. X110.

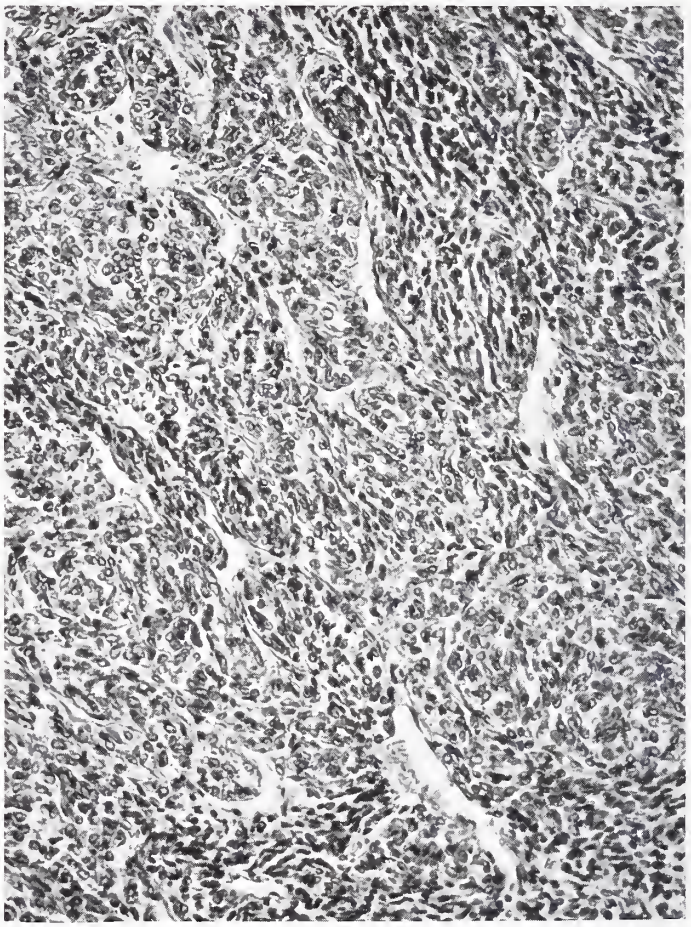


Figure 104
SYNOVIAL SARCOMA
This presumed primary synovial sarcoma of the heart is composed of large polygonal cells that grow in cords. Frequently, these cells are oriented around slitlike spaces lined by spindle-shaped cells. X195.

systolic ejection murmur which was thought to represent pulmonic stenosis. At necropsy, a 15 by 10 cm. tumor was found at the base of the heart, involving the pericardium and invading the outflow tract of the right ventricle and the pulmonary artery. The tumor extended into the right ventricle, obstructing the pulmonary valve. No metastases were found.

Microscopically, the tumor had the classic biphasic pattern (fig. 104) and staining properties characteristic of synovial sarcoma. Mesotheliomas may also exhibit a biphasic pattern; however, the staining properties and deep invasion into the right ventricle by this tumor differs significantly from the mesotheliomas of the pericardium.

To our knowledge, this is the only reported case of synovial sarcoma primary in the heart.

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METASTATIC TUMORS OF THE HEART AND PERICARDIUM

Metastatic tumors are the most frequently encountered cardiac tumors. The incidence of secondary tumors of the heart and pericardium is 20 to 40-fold greater than both benign and malignant primary cardiac tumors. Cardiac metastases are not uncommon findings at necropsy, and are reported from virtually every known malignant neoplasm with the possible exception of tumors primary to the central nervous system. In selected necropsy series which include only patients with metastatic malignant neoplasms, the incidence of cardiac metastases ranged from 10 to 20 percent.

Clinical Aspects. Although the vast majority of patients with metastatic tumors in the heart and pericardium appear to be without symptoms, such observations are deceiving because most patients with metastatic cardiac involvement have widespread metastatic disease and are often gravely ill. Cardiac findings are sometimes overlooked or clinically unimportant in the face of overwhelming multisystem disease. When specifically looked for, however, cardiac findings are present in a high percentage of patients with metastatic tumors and are often the first clue to cardiac involvement.

In general, cardiac findings associated with metastasis to the heart and pericardium form a tetrad: (1) Unexplained rapid cardiac enlargement; (2) symptoms of cardiac decompensation; (3) congestive heart failure; and (4) cardiac arrhythmias. Although none of these findings are specific, together they should alert the clinician to the possibility of cardiac metastases.

More specifically, cardiac findings associated with involvement of the heart and pericardium by metastatic neoplasms depend on the area of the heart involved and, to some extent, on the site of the primary tumor. Carcinoma of the lung and the breast, for example, tends to involve the pericardium, often without involving the heart; other tumors, notably melanoma and leukemia, involve the heart and/or heart and pericardium, but rarely metastasize only to the pericardium (Tables 24 and 25).

Approximately 25 percent of patients with metastatic involvement of the pericardium have significant impairment of cardiac function. Pericardial effusions are the most common cardiac findings. Cardiac enlargement on chest roentgenograms and, sometimes, pericardial friction rubs are helpful clinical findings. A large percentage of patients with pericardial metastases have pericarditis at necropsy, and clinical findings of constrictive pericarditis are occasionally noted. Cardiac tamponade is the most frequent cause of death in patients with significant impairment of cardiac function and pericardial metastases. Right-sided congestive heart failure is frequent. Major electrocardiographic changes include S-T segment depression, T wave abnormalities, and sinus tachycardia in 10 to 15 percent of all patients with pericardial metastasis. Arrhythmias, although rare with pericardial involvement, do occur and are usually atrial in origin.

Arrhythmias are the most prevalent manifestations of myocardial involvement, and the most common include atrial fibril-

lation or flutter, paroxysmal atrial tachycardia, nodal rhythms, heart block, and ventricular tachycardia and fibrillation. These arrhythmias are more dependent on tumor location than on tumor size, although the metastasis need not involve the atrial or ventricular septum to be associated with an arrhythmia. The sudden appearance of an arrhythmia in a patient with a malignant tumor is often a clue to diagnosis of metastatic involvement of the myocardium. Cardiac decompensation and congestive heart failure are the second most common manifestations of myocardial

TABLE 24

METASTATIC TUMORS OF THE HEART AND PERICARDIUM*

Primary Tumor	Total Cases	Cases with Metastases to Heart, Parietal Pericardium, or Both	Percentage of cases with Metastases to Heart, Parietal Pericardium, or Both
Leukemia	99	46	46
Melanoma	41	15	37
Carcinoma of thyroid	20	6	30
Carcinoma of lung	553	156	28
Sarcomas **	69	18	26
Carcinoma of esophagus	107	25	23
Carcinoma of kidney	53	12	23
Lymphomas †	245	55	22
Carcinoma of breast	492	104	21
Carcinoma of pancreas	96	14	15
Carcinoma of endometrium	69	8	12
Carcinoma of larynx	66	7	11
Transitional cell carcinoma ‡	81	6	7
Carcinoma of cervix	187	13	7
Carcinoma of stomach	212	14	7
Carcinoma of oral cavity	146	9	6
Carcinoma of liver and biliary system	75	4	5
Carcinoma of ovary	139	7	5
Myeloma	41	2	5
Carcinoma of colon and rectum	273	13	5
Carcinoma of prostate	123	5	4
All others	61	7	12
Total	3248	546	17

*This series was compiled from 3877 autopsies on patients with malignant tumors (excluding 162 patients without evidence of malignancy at the time of autopsy or with intracranial neoplasm) done between 1950 and 1970 at the Francis Delafield Hospital Division, Columbia-Presbyterian Medical Center, New York, N. Y., while one of us (JJF) was a resident.

**Includes both soft tissue and skeletal sarcomas. The frequency of cardiac metastasis was nearly identical, irrespective of the histologic classification.

†Includes all lymphomas, including reticulum cell sarcoma and Hodgkin's disease. The incidence of metastasis to the heart and pericardium was slightly higher than average for reticulum sarcoma (28%) and considerably lower for Hodgkin's disease (8%).

‡Includes tumors of the urethra, urinary bladder, ureter, and renal pelvis.

involvement. Early signs of myocardial replacement by metastatic tumor include gallop rhythms, pulsus alternans, and alternation of the intensity of heart sounds. Findings become more prominent with more extensive myocardial involvement and include: congestive heart failure, both left and right-sided; cardiomegaly on chest roentgenogram, often of unusual configuration; and nonspecific S-T segment and T wave changes on electrocardiogram. Any of these findings in a patient with a known malignant tumor suggests metastatic myocardial involvement.

Metastatic tumors may be largely or totally intracavitary; this occurs very rarely, usually following implants of tumor cells on the cardiac valves or endocardium. Systolic murmurs, often of changing intensity, and findings suggestive of obstruction of blood flow by occlusion of a valve orifice are frequent. Direct valvular involvement is frequent and may result in findings suggestive of stenosis or insufficiency. The presence of findings of valvular insufficiency may help to distinguish a metastatic or primary malignant intracavitary cardiac tumor from the more common benign intracavitary cardiac tumors, especially from cardiac myxoma.

Patients with metastatic tumors occasionally develop symptoms of acute myo-

TABLE 25

METASTATIC TUMORS OF THE PARIETAL PERICARDIUM

Primary Tumor	Total Cases	Cases with Metastasis to Parietal Pericardium	Percentage with Metastasis to Parietal Pericardium
Carcinoma of thyroid	20	3	15
Carcinoma of lung	553	80	15
Carcinoma of breast	492	61	12
Sarcomas *	69	8	12
Carcinoma of kidney	53	4	8
Carcinoma of pancreas	96	6	6
Carcinoma of esophagus	107	6	6
Lymphoma †	245	13	5
Melanoma	41	2	5
Carcinoma of endometrium	69	3	4
Carcinoma of ovary	139	6	4
Carcinoma of stomach	212	8	4
All others	1152	16	1
Total	3248	216	7

*Includes both soft tissue and skeletal sarcomas. The frequency of pericardial metastasis was nearly identical, irrespective of the histologic classification.

†Includes all lymphomas including reticulum cell sarcoma and Hodgkin's disease. The frequency of pericardial metastasis was nearly identical, irrespective of the histologic classification.

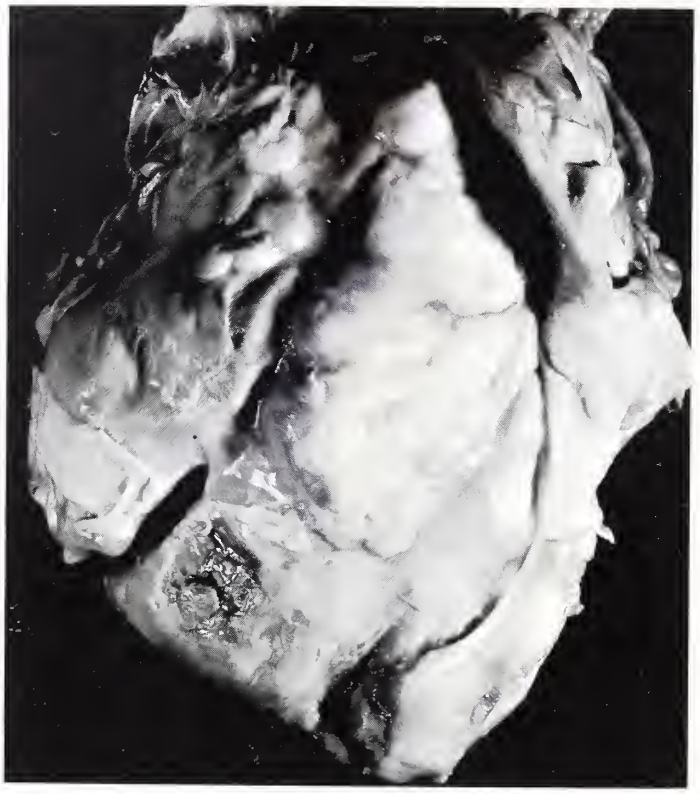

Figure 105
METASTATIC CARCINOMA
This illustrates the direct extension of a carcinoma of the lung to the parietal and visceral pericardium. The heart is encased in tumor; grossly, it is reminiscent of a mesothelioma of the pericardium.

cardial infarction. The myocardial infarct may be secondary to tumor emboli from an intracavitary tumor, or result from invasion or compression of a coronary artery by a tumor mass. Although reported in the literature, this is decidedly unusual in patients with metastatic tumors of the heart and pericardium.

Pathology. Nearly every type of malignant tumor from every organ and tissue has been reported to metastasize to the heart. Perhaps the sole exception would be tumors primary to the central nervous system. Tables 24 and 25 summarize the frequency of metastasis of the most common malignant neoplasms to the heart and pericardium and to the pericardium alone. In addition, in the files of the AFIP are cases of carcinoid, seminoma, choriocarcinoma, malignant teratoma, thymoma, and pheochromocytoma metastatic to the heart. The data in this section are drawn exclusively from adults. However, in the AFIP files there are also cases of Wilm's tumor, neuroblastoma, lymphomas, and leukemias in children, metastatic to the heart and pericardium.

Forms of metastatic growth in the heart and pericardium are somewhat dependent on the mode of spread and the origin of the tumor. When the pericardium is solely involved (Table 25), especially by carcinoma of the lung, breast, and esophagus, the tumor frequently involves the pericardium by direct extension from contiguous structures (fig. 105). In this instance,

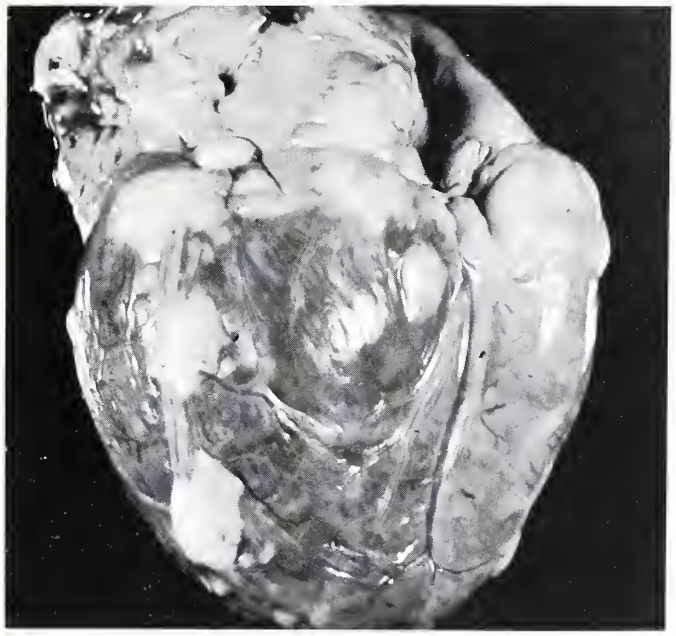

Figure 106
METASTATIC CARCINOMA

This carcinoma metastasized to the visceral pericardium from a primary tumor in the lung. The tumor nodules are well circumscribed and confined to the pericardium. When the primary site is not adjacent to the pericardium, malignant cells usually reach the heart via retrograde lymphatic spread.

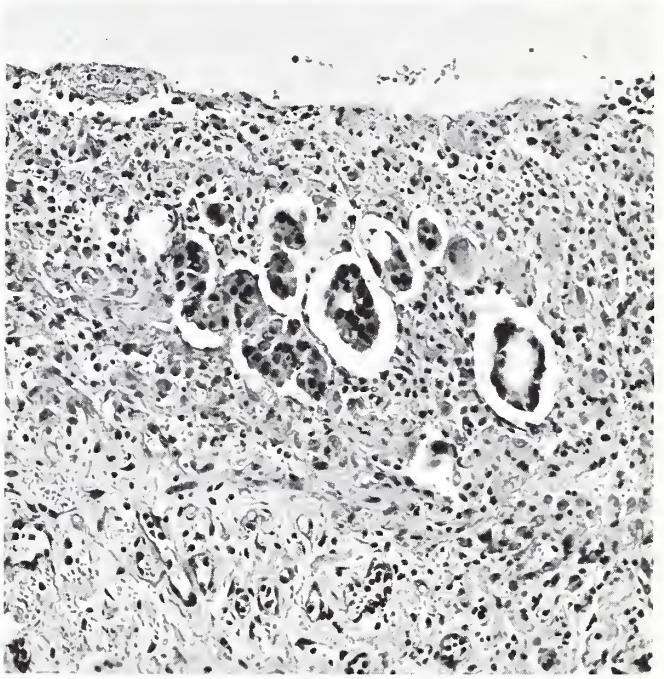

Figure 107
METASTATIC CARCINOMA

Small, vascular channels in the pericardium, presumably lymphatic channels, are dilated and filled with malignant cells. If carefully searched for, lymphatic channels filled with malignant cells can be found in almost all metastatic carcinomas involving the heart, especially when the primary site is in the lung or breast. In this patient, the primary site was in the lung. X145.

the pericardium is usually diffusely involved.

In approximately 50 percent of the patients with carcinoma of the lung and breast with cardiac metastasis, the primary tumor is far removed from the heart (fig. 106). There is no evidence of direct extension of the primary tumor to involve the heart; rather frequently, however, there is evidence of retrograde lymphatic spread of the tumor to the heart and pericardium. Tumor-filled lymphatic channels in the pericardium, at the base of the heart and in the anterior mediastinum, can usually be found after diligent search (fig. 107). Most carcinomas appear to reach the heart and pericardium by retrograde lymphatic spread, and multiple small nodules, many of microscopic size, are found throughout the heart and pericardium. Solitary metastatic tumor nodules are infrequent; usually, multiple microscopic foci are also present.

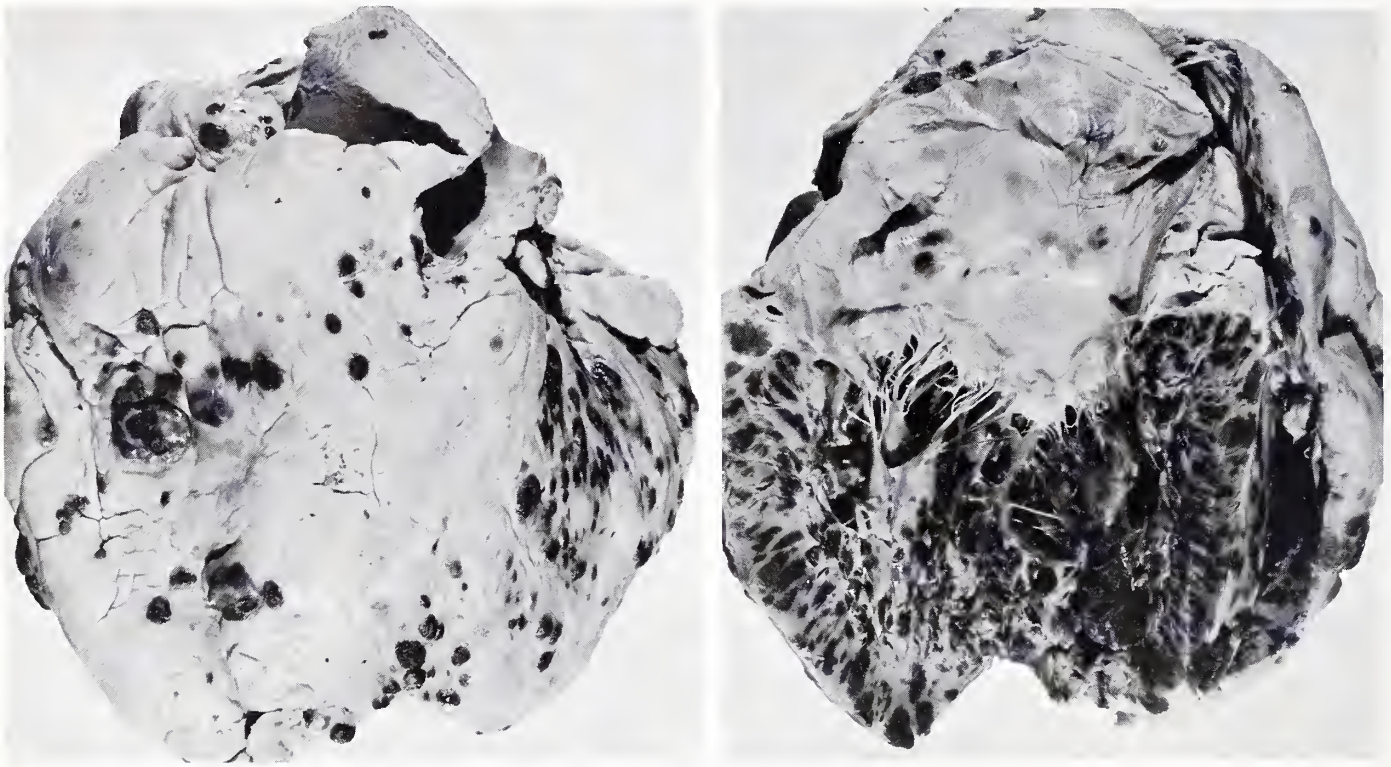

Figure 108
METASTATIC MALIGNANT MELANOMA
Dark tumor nodules are clearly seen; they replace a large percentage of the myocardium in this metastatic involvement of the heart and pericardium from malignant melanoma. Malignant melanoma and most sarcoma cells usually reach the heart via the blood stream.

Besides direct extension from contiguous structures and lymphatic spread, carcinoma may occasionally reach the heart via direct venous extension, especially renal cell carcinoma and hepatoma, which may extend up the inferior vena cava into the right atrium. Hematogenous spread, while unusual for carcinoma, is the main route of metastases for sarcoma, lymphoma, and leukemia, as well as melanoma involving the heart (fig. 108). Among this group of neoplasms, the metastatic sites and type of involvement in the heart are dependent on the primary tumor. Leukemia, lymphomas, particularly lymphosarcoma (fig. 109), and certain sarcomas, notably angiosarcoma, tend to involve the heart and pericardium diffusely, often covering the parietal pericardium and epicardium with sheets of malignant cells. Parietal pericardial involvement, in the absence of myocardial metastasis, is distinctly unusual (Table 25). Multiple metastatic nodules and occasional tumor emboli can be demonstrated in melanomas, most sarcomas, and multiple myeloma.

Metastatic tumor growth in the heart is generally solid, small, and multiple (fig. 110); large tumor masses or confluent tumor nodules are rare, and tumor necrosis is extremely unusual. Tumor nodules may occur anywhere in the heart (fig. 111) and have been reported in the atrioventricular node, His bundle, and bundle branches. The clinical presence of arrhythmias, however, does not correlate absolutely with the finding of metastatic nodules in the conduction system.

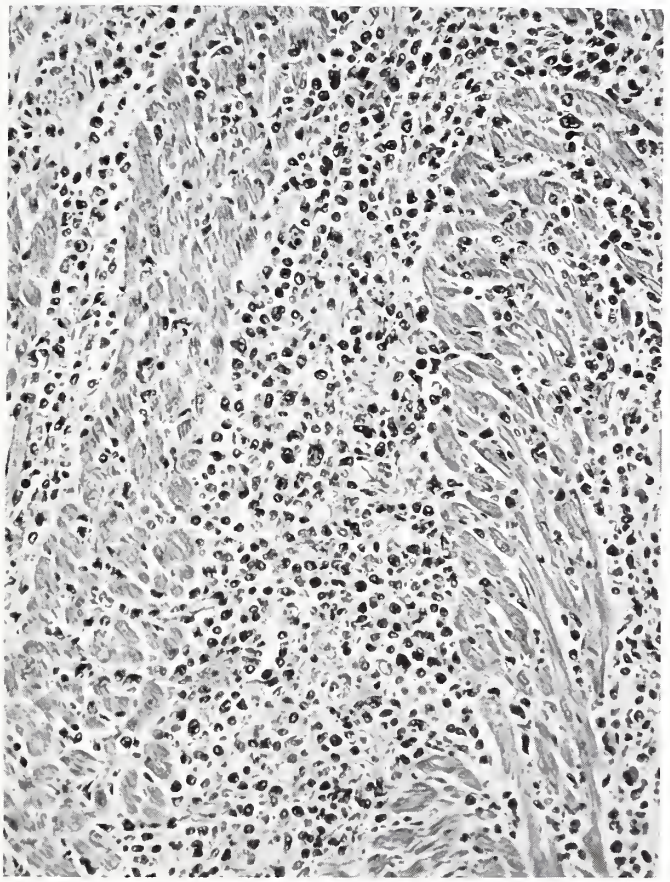

Figure 109
METASTASIS FROM MALIGNANT LYMPHOMA

Involvement of the heart in malignant lymphoma is usually diffuse. In the heart, primary and metastatic lymphomas are identical; only the absence of extracardial involvement distinguishes primary cardiac lymphomas from metastatic lymphomas. Hematogenous spread is the most likely route for involvement of the pericardium and heart by lymphomas and leukemias. Cardiac involvement in chronic lymphocytic leukemia is similar histologically to metastasis from malignant lymphoma. X165.

Figure 110
METASTATIC CARCINOMA

Multiple nodules of malignant cells throughout the pericardium and myocardium are often found when the heart is involved by metastatic carcinoma. Nodules of metastatic papillary carcinoma of the thyroid are apparent macroscopically in this heart. More frequently, however, the metastases are microscopic and must be carefully searched for. Cardiac metastases from carcinoma, are usually well circumscribed, both macroscopically and microscopically.

Figure 111
METASTATIC MULTIPLE MYELOMA
(PLASMACYTOMA)

Multiple myeloma (plasmacytoma) metastasized to the right atrium in a patient with extensive bony involvement. A portion of the tumor mass protrudes into the atrial cavity, but the tumor also infiltrated the atrial wall.

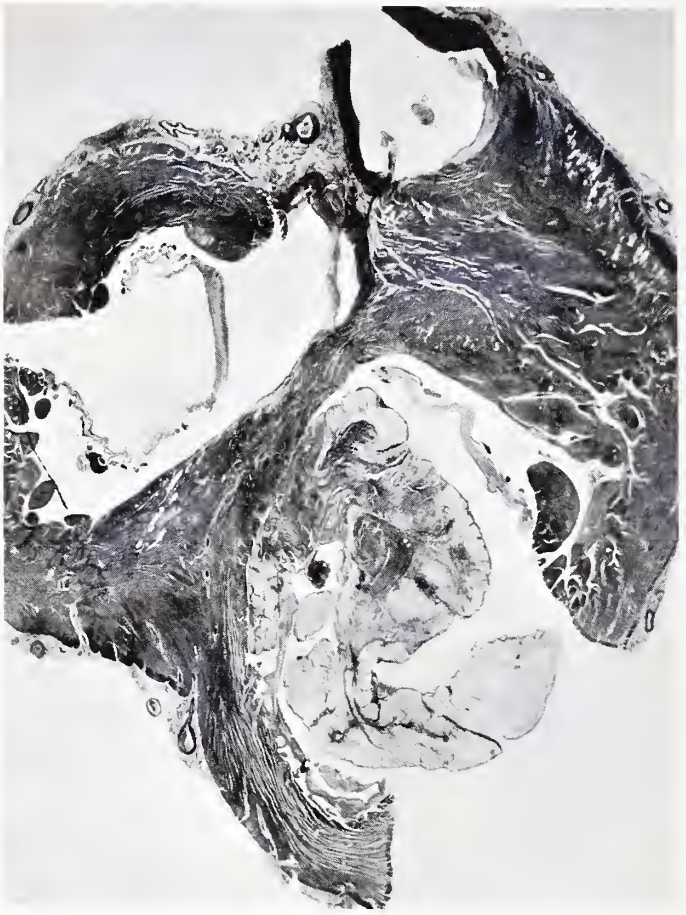

Figure 112
METASTATIC LIPOSARCOMA

This metastatic implant on the endocardium of the ventricular septum is from a liposarcoma primary in the retroperitoneum. The tumor mass is almost entirely intracavitary and has not invaded the septal myocardium. Macroscopically, the tumor resembles a cardiac myxoma. The microscopic appearance of the tumor and the clinical history of the patient belie such a diagnosis, and emphasize the importance of a complete clinical history and extensive histologic examination of every suspected primary tumor of the heart.

Metastatic tumors, especially sarcoma, must be distinguished from primary tumors of the heart and pericardium (fig. 112). Usually, this distinction is simple, based on histologic and clinical evaluation. Metastatic sarcoma is frequently a late manifestation of a known primary tumor. Mesothelioma is the one notable exception. Pericardial and pleural mesotheliomas are identical histologically, and it is virtually impossible to determine their site of origin. Mesothelioma is discussed under primary malignant tumors of the heart and pericardium. That discussion was limited to tumors confined to, or clearly derived from the pericardium, but the more common pleural mesotheliomas frequently involve the pericardium. They are often clinically indistinguishable from, as well as morphologically identical to pericardial mesothelioma.

Treatment. Treatment of tumors metastatic to the heart is generally symptomatic and aimed at controlling arrhythmias and

managing congestive heart failure. Radiation therapy and chemotherapy have been used to control cardiac metastasis as well as the primary tumor. Radiation therapy has been most successful in controlling pericardial effusions associated with metastatic involvement of the pericardium.

Cardiac findings, similar to those of metastatic involvement of the heart, may result from radiation therapy and chemotherapy; they are secondary to direct cardiac toxicity of some of these agents.

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PRIMARY TUMORS OF MAJOR BLOOD VESSELS

Tumors arising in major blood vessels are distinctly uncommon. Since the first reports of "venous tumors" in the 1860's, approximately 170 examples of primary tumors, both benign and malignant, of major blood vessels have been published. The incidence of primary tumors of blood vessels is approximately 20 percent of the incidence of primary tumors of the heart and pericardium. The 12 examples of primary tumors of major blood vessels in the AFIP collection are summarized in Table 26.

The majority of tumors of the major blood vessels are of smooth muscle origin. Leiomyomas and leiomyosarcomas account

TABLE 26

TUMORS OF MAJOR BLOOD VESSELS
12 TUMORS IN THE AFIP COLLECTION

Age of Patient	Sex of Patient	Diagnosis	Site	Remarks
Veins				
20 yrs	F	Leiomyoma	Lesser saphenous vein	Surgical excision
31 yrs	M	Leiomyoma	Cervical vein	Surgical excision
41 yrs	M	Leiomyosarcoma	Greater saphenous vein	Surgical excision with recurrence
44 yrs	F	Leiomyoma	Vein of foot	Surgical excision
50 yrs	M	Leiomyosarcoma	Lesser saphenous vein	Surgical excision with recurrence
51 yrs	F	Leiomyosarcoma	Inferior vena cava	Autopsy
52 yrs	F	Leiomyoma	Lesser saphenous vein	Surgical excision
55 yrs	M	Leiomyoma	Radial vein	Surgical excision
63 yrs	M	Leiomyosarcoma	Anticubital vein	Surgical excision
Arteries				
22 yrs	F	Fibrosarcoma	Thoracic aorta	Surgical excision with recurrence
36 yrs	M	Chondrosarcoma	Pulmonary artery	Invasion aorta and mediastinum
64 yrs	M	Leiomyosarcoma	Right iliac artery	Surgical excision attempted

for 70 percent of all reported cases and over 90 percent of tumors arising in large veins.

PRIMARY TUMORS OF LARGE VEINS

Approximately 65 percent of all primary tumors of major blood vessels arise in large veins.

Clinically, the signs and symptoms associated with tumors arising in veins are related to obstruction of venous blood flow; however, the magnitude of the clinical findings is directly related to the location of the tumor. Peripheral tumors are associated with a visible or palpable mass, pain or tenderness over the mass, swelling of the extremity distally, and evidence of venous collaterals beneath the skin. Central tumors, or tumors in the inferior vena cava, are associated with characteristic clinical findings, depending on their location. Patients with tumors in the upper third of the inferior vena cava, from the entrance of the hepatic veins to the right atrium, usually have ascites, peripheral edema, hepatomegaly, and albuminuria, and develop superficial venous collaterals (caput medusa). Clinical findings associated with tumors in the middle third, from the entrance of the renal veins to the entrance of the hepatic veins, are peripheral edema, usually followed by the appearance of

TABLE 27

LEIOMYOMAS PRIMARY IN LARGE VEINS*

Year	Reported by	Age of Patient	Sex of Patient	Diagnosis	Site
1869	Boettcher	30 yrs	F	Myoma	Ulnar vein
1896	Cornil	—	—	Myoma	Vein of arm
1903	Cernezzi	60 yrs	M	Fibroleiomyoma	Spermatic vein
1913	Niederle	—	—	Leiomyoma	Basilic vein
1914	Schnyder	27 yrs	F	Leiomyoma	Marginal vein of foot
1917	Ecoffey	40 yrs	M	Fibroleiomyoma	Saphenous vein
1923	Natali	68 yrs	M	Fibroleiomyoma	Femoral vein
1927	Marri	45 yrs	M	Fibroleiomyoma	Axillary vein
1932	Kaplan	3½ yrs	—	Leiomyofibroma	Pulmonary vein
1950	Klein and Bandzak	57 yrs	F	Leiomyofibroma	Vein of foot
1958	DeWeese	54 yrs	M	Leiomyoma	Saphenous vein
1960	Macek	54 yrs	M	Leiomyoma	Inferior vena cava
1964	Salaquarda	34 yrs	F	Cellular leiomyoma	Inferior vena cava
1964	Kerr	32 yrs	F	Leiomyoma	Basilic vein
1971	Wilder	55 yrs	M	Leiomyoma	Saphenous vein
1974	Mandelbaum	52 yrs	F	Leiomyoma	Inferior vena cava

*Excluding those accepted by Kevorkian and Cento as probable examples of leiomyosarcoma.

superficial venous collaterals, albuminuria, and, occasionally, edema of the abdominal wall. With tumors in the lower third of the inferior vena cava, below the renal veins, venous collaterals usually appear over the groin and lower abdomen; however, peripheral edema and albuminuria are not present. Only one tumor primary in the superior vena cava has been reported.

Histologically, over 90 percent of tumors arising in large veins are of smooth muscle origin. Only 10 tumors of non-smooth muscle origin have been reported, and these case reports are listed in the references.

Leiomyoma

Approximately 16 percent of smooth muscle tumors of the veins are benign. Sixteen leiomyomas arising in veins have been reported since 1869 (Table 27). In addition, there are five examples of leiomyoma arising in veins in the AFIP collection (Table 26). The incidence is about equally divided between males and females in the 21 patients, who ranged in age from 3½ to 68 years (two-thirds of the patients were between 30 and 60 years of age). Seven leiomyomas were located in the upper extremities, 10 in the lower extremities (fig. 113), and four were situated centrally (vena cavae or pulmonary veins).

Microscopically, leiomyomas are composed of haphazardly arranged bundles of elongated cells, resembling normal smooth muscle cells (fig. 114). The nuclei are

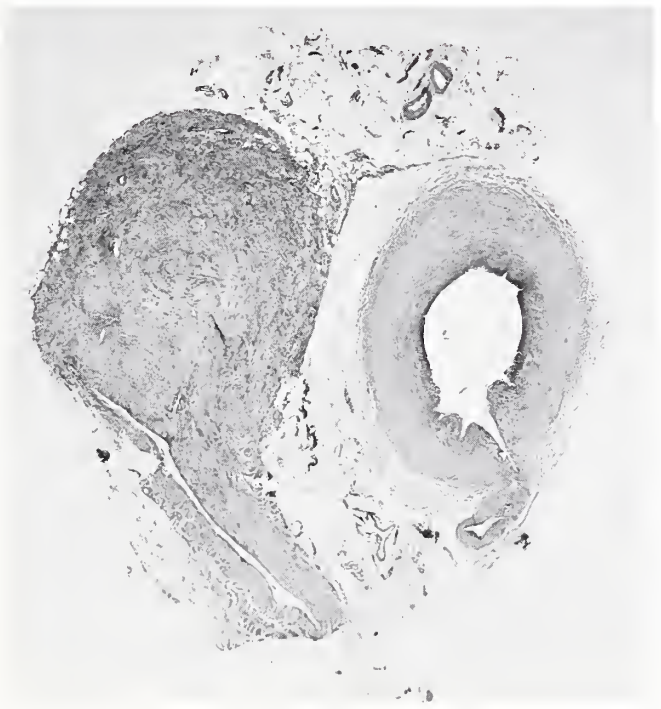


Figure 113
LEIOMYOMA
(Figures 113 and 114 from same case)
This leiomyoma arose in the wall of a vein. X15.

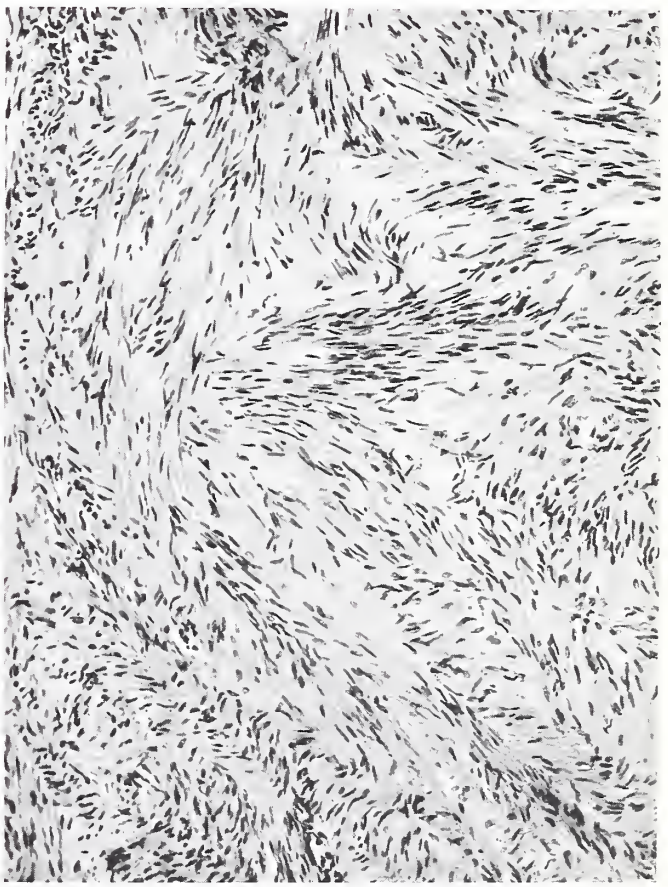


Figure 114
LEIOMYOMA
The leiomyoma in figure 113 is composed of haphazardly arranged bundles of normal appearing smooth muscle cells. Nuclear palisading is often striking, and with trichrome stains, cytoplasmic filaments are easily distinguishable. X110.

blunt-ended and regular in appearance. With special stains, especially Masson's trichrome stain, filaments thought to represent myofibrils are readily apparent in the cytoplasm of the cells of leiomyoma, and extracellular collagen is scant.

Leiomyosarcoma

The majority of smooth muscle tumors of large veins are malignant. In fact, slightly more than 75 percent of all benign and malignant tumors arising in large veins are leiomyosarcomas. In 1973, Kevorkian and Cento published a comprehensive review of all leiomyosarcomas of major blood vessels. They accepted 68 leiomyosarcomas in large veins from the world literature. Since then, there have been 15 additional reports in the literature (see reference list for case reports); Table 26 lists four of these tumors that are in the AFIP collection. The additional 19 patients reaffirm the observations of Kevorkian and Cento. Approximately half the leiomyosarcomas of the large veins arise in the inferior vena cava; they occur almost exclusively in women, outnumbering men by 8 to 1. Although this tumor has been reported in patients from 24 to 83 years of age, 40 percent of patients are in their seventh decade of life.

Figure 115
LEIOMYOSARCOMA
(Figures 115–117 from same case)
This leiomyosarcoma arose in the great saphenous vein. The tumor appears encapsulated. On cross-section, the mass is firm and the lumen of the vein is not readily discernible.

By contrast, the incidence of leiomyosarcoma arising in large veins other than the inferior vena cava (fig. 115) is nearly equal for males and females; patients ranged in age from 3½ to 76 years, with no peak age. Veins of the lower extremity are most frequently involved (60 percent), followed by veins of the torso (25 percent) and the upper extremities and head and neck (15 percent).

Microscopically, malignant smooth muscle tumors consist of elongated cells, with blunt-ended nuclei arranged in interlacing bundles and cords (figs. 116, 117). Occasionally, there may be a suggestion of nuclear palisading. There may be considerable cellular anaplasia and marked nuclear pleomorphism, often with large bizarre nuclei and, occasionally, multinucleated forms (fig. 118). The mitotic rate is usually elevated. These features help to distinguish leiomyoma from leiomyosarcoma. Occasionally, the only absolute criterion is the presence of metastases. Although the cytoplasm of the cells of leiomyosarcoma is deeply eosinophilic and collagen is absent

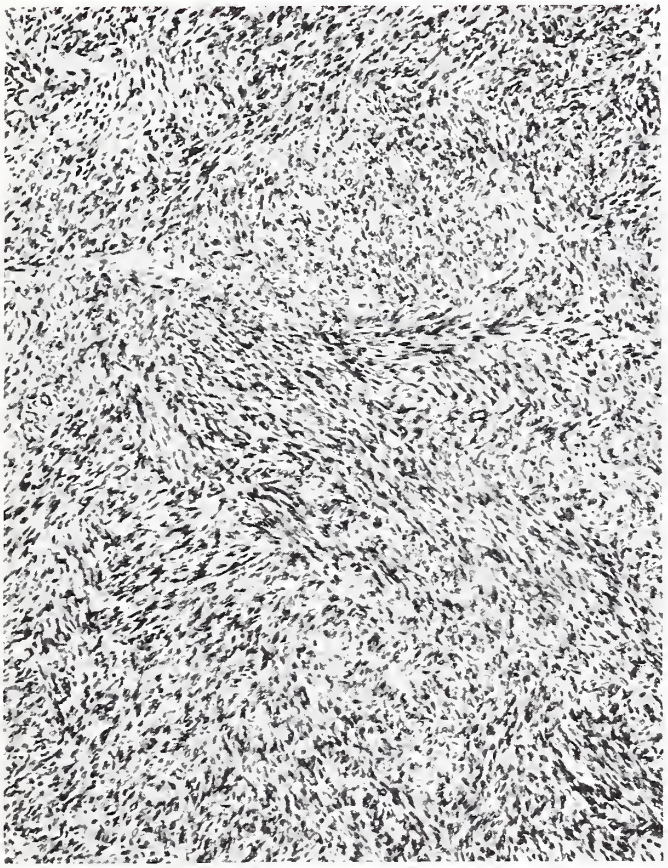


Figure 116
LEIOMYOSARCOMA

Cells of the leiomyosarcoma shown in figure 115 grow in interlacing cords. The nuclei are blunt-ended, and, frequently, there is the suggestion of nuclear palisading. Collagen is scant or absent in leiomyosarcomas; however, reticulin fibers, running parallel to the long axis of the tumor cells, are usually prominent with reticulum stains. X90.

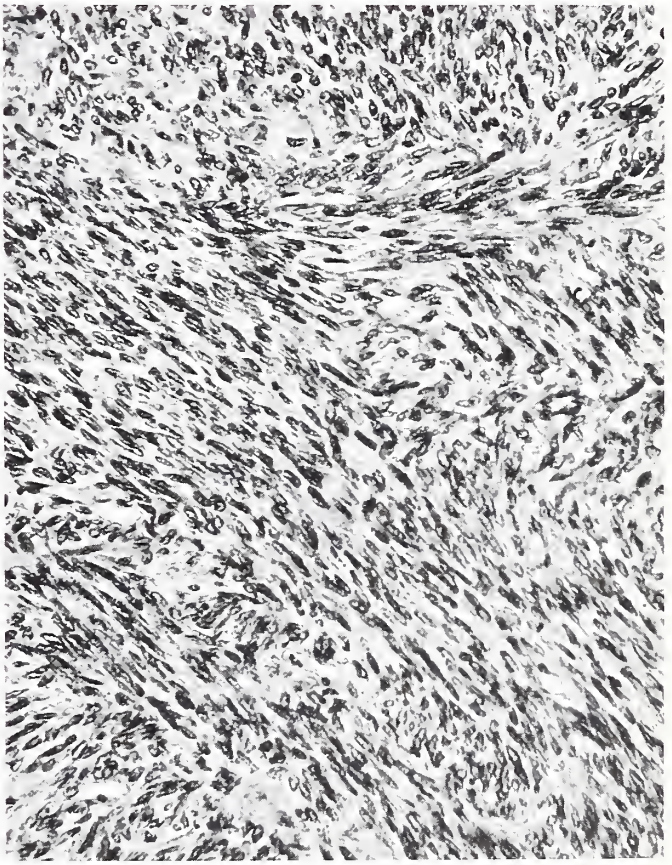


Figure 117
LEIOMYOSARCOMA

Closely packed spindle cells of the leiomyosarcoma in figure 115 have abundant cytoplasm, which stains red to red-purple with Masson's trichrome. It is seldom possible to demonstrate distinct myofibrils. The intercellular stroma is scanty. Mitotic activity, usually elevated, is one of the criteria of malignancy in smooth muscle tumors. X195.

or scant in the stroma, myofibrils are not usually identifiable by light microscopy. By electron microscopy (fig. 119), the cytoplasm contains scattered bundles of myofibrils which have characteristic spindle-shaped densities similar to smooth muscle. The cells are surrounded by a well defined basement membrane, and large numbers of pinocytotic vesicles and occasional marginal dense bodies may be seen along the plasma membrane.

Treatment. Surgical excision is the treatment of choice for both leiomyoma and leiomyosarcoma of the large veins. In the past, prognosis for those patients with leiomyosarcoma was generally poor, but recent surgical literature suggests that long survivals and even cures are possible with early diagnosis and complete surgical resection.

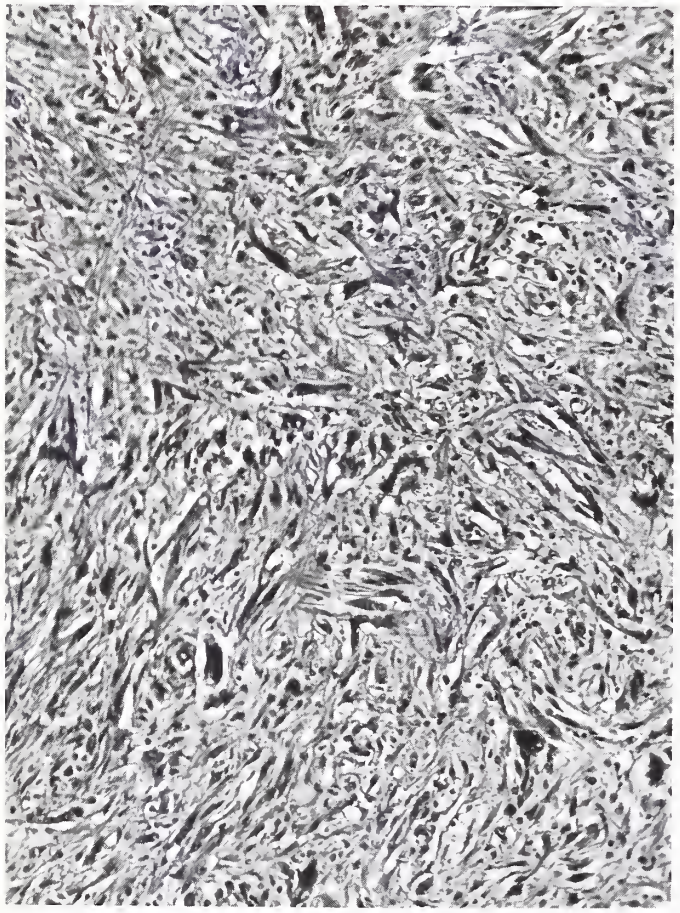


Figure 118
LEIOMYOSARCOMA OF THE INFERIOR VENA CAVA
(Figures 118 and 119 from same case)

Areas of marked nuclear atypia, cellular pleomorphism, and elevated mitotic activity are often encountered in leiomyosarcoma. Smooth muscle cells retain some degree of differentiation and have deeply eosinophilic cytoplasm and a suggestion of nuclear palisading. Occasionally, the entire tumor is pleomorphic. More frequently, however, areas of cellular pleomorphism and nuclear atypia merge with the more classical appearance of the leiomyosarcoma illustrated in figures 116 and 117. X115.

PRIMARY TUMORS OF LARGE ARTERIES

Primary tumors of large arteries are extremely unusual; about 70 have been reported. With few exceptions, all reported tumors were malignant. Case reports of benign tumors of the large arteries are included in the references. Since the validity of such reports is unclear, we will discuss only malignant tumors of the large arteries in this section.

Primary Malignant Tumors of the Pulmonary Artery

In 1969, Wackers and associates reviewed the world literature and collected 21 examples of primary sarcoma of the pulmonary trunk. Included were tumors which involved the pulmonary valve, but not the right ventricle. To 1975, there were 22 additional reports in the literature (Table 28), and one such tumor in the AFIP collection (Table 26).

Sarcoma of the pulmonary trunk occurs more frequently in women (65 percent), often during the sixth and seventh decades of life—60 percent of patients were between 50 and 65 years of age. Clinical signs and symptoms are frequently confusing

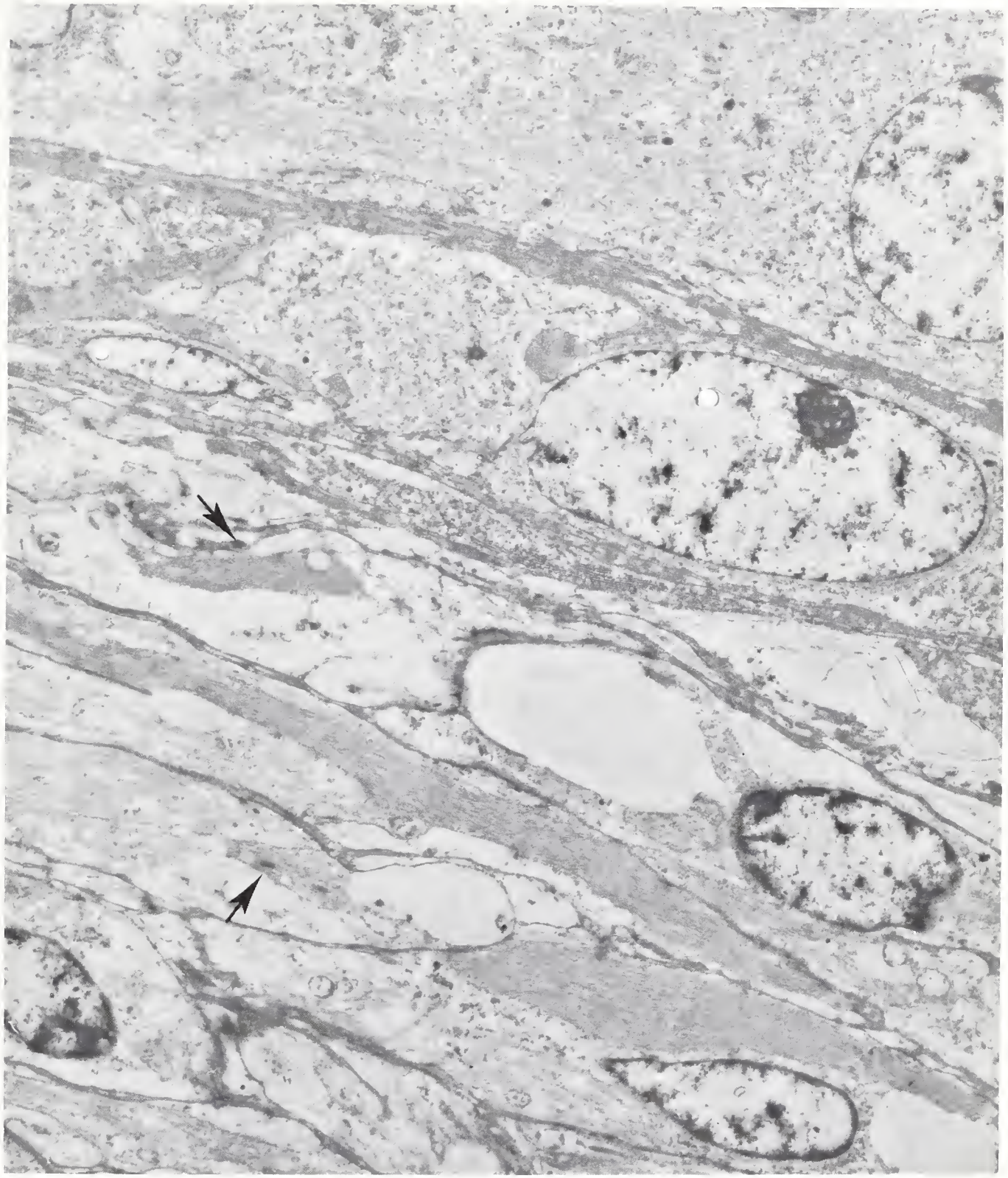


Figure 119
LEIOMYOSARCOMA OF THE INFERIOR VENA CAVA

By electron microscopy, the cells of the leiomyosarcoma in figure 118 are filled with myofibrils which usually course along the long axis of the cell. Characteristically, spindle-shaped densities are found along the myofibrils, and marginal dense bodies are found against the cell membrane (arrows). Unlike fibroblasts, cells of leiomyosarcoma have a prominent, well developed basement membrane. Uranyl acetate and lead citrate stain, X13,980.

and nonspecific. Most patients first seek medical advice because of progressive congestive heart failure of sudden onset. Congestive heart failure is usually refractory to medical management. In addition, a precordial systolic murmur, often of low intensity, is present in approximately half the patients. Dyspnea, cyanosis, hemoptysis, and polycythemia are other reported symptoms in patients with sarcoma of the pulmonary trunk.

This tumor appears to arise in the main pulmonary artery, and may grow in a retrograde fashion, involving the pulmonary valve, or extend along branches of the pulmonary artery into the lung. Histologically, about one-fourth of the sarcomas of the pulmonary artery are leiomyosarcomas—there have been nine published cases and three additional early cases accepted by Kevorkian and Cento as probable leiomyosarcoma. In reported cases, undifferentiated sarcoma and fibrosarcoma together account for more than 50 percent of the diagnoses. On critical review, however, it is probable that 25 to 50 percent of such cases actually represent leiomyosarcomas. Angiosarcoma, rhabdomyosarcoma, osteosarcoma, chondrosarcoma, and malignant mesenchymoma primary in the pulmonary trunk have also been reported.

TABLE 28

PRIMARY MALIGNANT TUMORS OF THE PULMONARY ARTERY

Year	Reported by	Age of Patient	Sex of Patient	Diagnosis
1949	Lowell and Tuhy	41 yrs	F	Chondrosarcoma
1962	Tiraspolskaya	35 yrs	F	Intimal sarcoma
1964	Goldstein and Joubert	51 yrs	M	Rhabdomyosarcoma
1965	Orell	61 yrs	M	Malignant mesenchymoma
		75 yrs	F	Angiofibromyxosarcoma
1968	Friedman and Smith	53 yrs	F	Leiomyosarcoma
1969	Cain	72 yrs	F	Spindle cell sarcoma
		62 yrs	F	Pleomorphic sarcoma
		32 yrs	M	Fibrosarcoma
1969	Nalbat	52 yrs	F	Angiosarcoma
1970	Hirsch	22 yrs	F	Undifferentiated sarcoma
1970	McConnell	53 yrs	F	Osteogenic sarcoma
1971	Breuer	51 yrs	F	Pleomorphic sarcoma
		52 yrs	F	Pleomorphic sarcoma
1971	Hausen and Kraus	32 yrs	M	Fibrosarcoma
		32 yrs	F	Undifferentiated sarcoma
1972	Busch	59 yrs	F	Fibromyxosarcoma
1972	Sethi	50 yrs	F	Sarcoma
1973	Altman and Shelley	64 yrs	F	Intimal sarcoma
1974	Hayes	52 yrs	F	Leiomyosarcoma
1974	Thijs	48 yrs	F	Leiomyosarcoma
1975	Roth	64 yrs	F	Sarcoma

Recently, Shmookler, Marsh, and Roberts reviewed pulmonary artery sarcomas. They reported two cases and collected an additional five cases from the recent literature. Including these seven cases, there are currently 50 sarcomas of the pulmonary artery and/or pulmonary valve in the world literature.

PRIMARY MALIGNANT TUMORS OF THE AORTA AND LARGE ARTERIES

Twenty-three malignant tumors, primary in the aorta or large arteries, have been reported (Table 29); there are two such tumors in the AFIP collection (Table 26). The ratio of men to women was

TABLE 29

23 PRIMARY MALIGNANT TUMORS OF THE AORTA AND LARGE ARTERIES

Year	Reported by	Age of Patient	Sex of Patient	Diagnosis	Site
1873	Brodowski	53 yrs		Sarcoma	Thoracic aorta
1891	Miura	38 yrs	M	Giant cell sarcoma	Thoracic aorta
1911	Auffermann	38 yrs	M	Spindle cell sarcoma (Kevorkian-Cento leiomyosarcoma)	Abdominal aorta
1913	Ferrarini	66 yrs	M	Sarcoma (Kevorkian-Cento leiomyosarcoma)	Left femoral artery
1925	Ajello	70 yrs	F	Leiomyosarcoma	Right femoral artery
1946	Nencki	47 yrs	M	Pleomorphic sarcoma	Abdominal aorta
1949	Giaccai	62 yrs	M	Fibrosarcoma	Splenic artery
1952	Karhoff	55 yrs	M	Endothelioma ?Intimal sarcoma	Thoracic aorta
1959	Kovaleva and Press	65 yrs	M	Pleomorphic sarcoma	Abdominal aorta
1960	Kattus	22 yrs	F	Fibromyxoma	Thoracic aorta
1963	Kaigorodova	62 yrs	F	Malignant endothelioma	Ascending aorta
1963	Courbier	64 yrs	M	Hemangiopericyto-sarcoma	Femoral artery
1963	Zeithofer	3½ mos	M	Fibromyxosarcoma	Thoracic aorta
1964	Sladden	64 yrs	M	Intimal sarcoma	Abdominal aorta
		59 yrs	M	Intimal sarcoma	Abdominal aorta
1965	Smeloff	65 yrs	F	Intimal sarcoma	Abdominal aorta
1965	Grohme	60 yrs	M	Myxomatous endothelioma	Abdominal aorta
1967	Sadlinski and Gruk	60 yrs	F	Leiomyosarcoma	Right femoral artery
1968	Hopkins	55 yrs	M	Leiomyosarcoma	Right common iliac artery
1968	Stevenson	60 yrs	M	Fibromyxosarcoma	Abdominal aorta
1972	Breborowicz	48 yrs	M	Angiosarcoma	Thoracic aorta
1972	Salm	57 yrs	F	Fibrosarcoma	Thoracic aorta
1973	Kevorkian and Cento	71 yrs	M	Leiomyosarcoma	Left femoral artery

almost 3 to 1, and 50 percent of the patients were over 60 years of age.

Clinically, patients with these tumors have signs and symptoms which are not necessarily suggestive of large vessel disease. Most patients complain of fever, malaise, weakness, and anorexia—nonspecific signs and symptoms of malignancy. Hypertension, renal colic, low back pain, and Leriche's syndrome have been reported in patients with sarcoma of the aorta or large arteries.

These sarcomas appear to arise in the wall of the vessel affected (pl. IX-A, B).

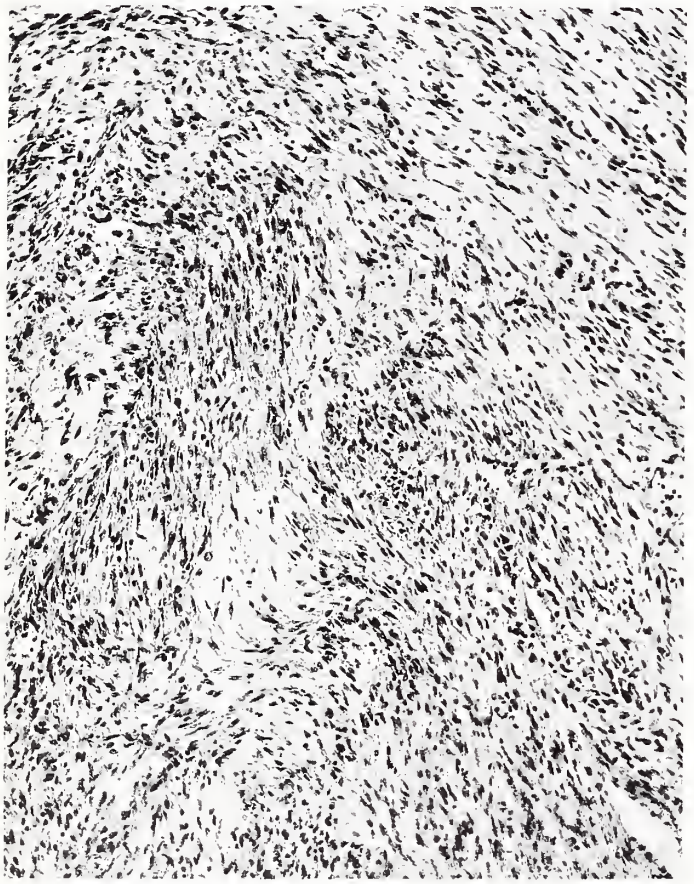


Figure 120
FIBROSARCOMA OF AORTA
(Figure 120 and Plate IX-A from same case)
A fibrosarcoma, primary in the thoracic aorta, is composed of bland appearing fibroblasts set in an abundant myxoid stroma. The entire wall of the aorta was replaced by the tumor. Histologically similar metastases were present in the lung. X100.

They rarely occlude the vessel lumen, but rather grow along the intimal surface. Many of these tumors are confined to the intimal layer of the blood vessel, without evidence of invasion of the muscular wall. Of the eight primary sarcomas arising in a large artery, seven were either reported as leiomyosarcoma or accepted by Kevorkian and Cento as probable examples of this entity.

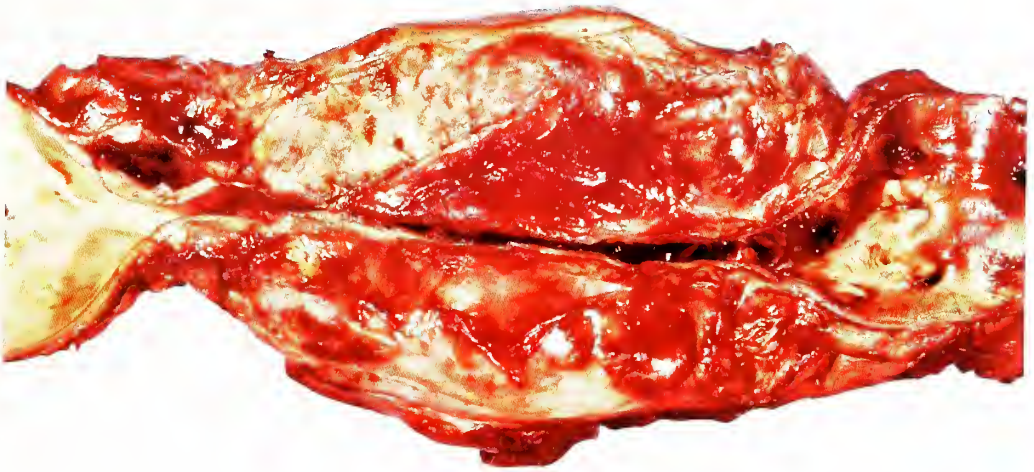
In the aorta, sarcomas were equally divided between the thoracic and abdominal regions. None of the primary aortic sarcomas were reported as leiomyosarcoma. These tumors were diagnosed as undifferentiated sarcoma, fibrosarcoma (fig. 120), or fibromyxosarcoma, and intimal or endothelial sarcoma. Their exact histogenesis is difficult to determine without the opportunity to have studied the tumors histochemically and by electron microscopy—technics which were not available to the authors of the majority of the reports.

Intimal Fibroplasia

Intimal fibroplasia (fig. 121) is part of the fibromuscular hyperplasia complex of arterial lesions in which the intima is primarily involved. The intima is variably thickened and replaced by loose myxomatous tissue (fig. 122), within which both proliferating fibroblasts and smooth muscle cells appear (fig. 123). The internal elastic membrane is often focally disrupted. Renal arteries are most frequently involved by this entity; however, intimal fibroplasia has also been reported in other large arteries, including the iliac, femoral, and carotid arteries, as well as the abdominal aorta. The area of the artery involved is variable and

PLATE IX

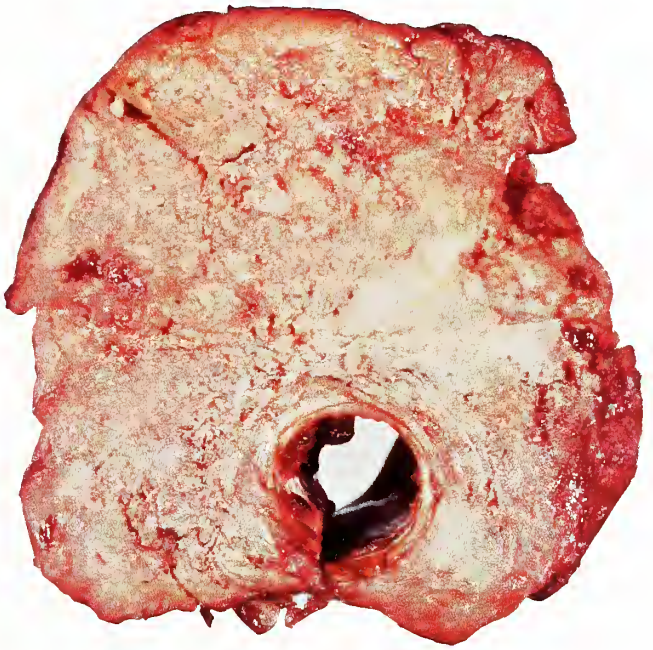
FIBROSARCOMA OF THE AORTA



(Plate IX-A and Figure 120 from same case)

A. In this primary fibrosarcoma of the aorta, the aortic wall is completely replaced by the tumor, although a portion of the lumen is retained.

METASTATIC TUMOR TO AORTA



B. Unlike primary tumors of great vessels, the wall of the great vessel, here the aorta, is usually spared by metastatic tumors. Although the tumor encroaches on the adventitia and outer third of the media, the remainder of the aortic wall is spared and the lumen is not compromised.

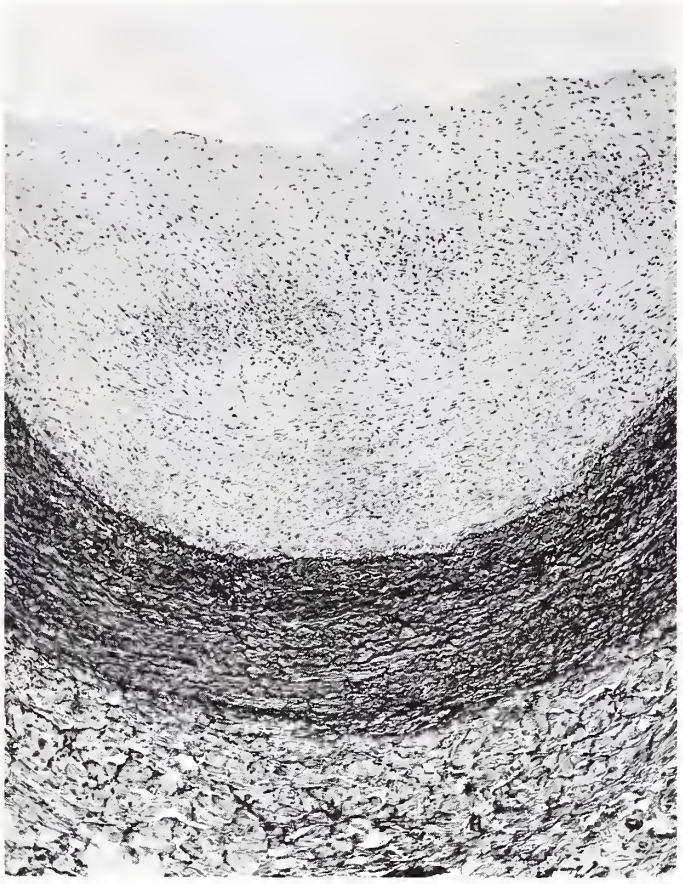


Figure 121
INTIMAL FIBROPLASIA OF THE AORTA
(Figures 121—123 from same case)
In large elastic arteries, this process is confined to the intima. Characteristically, there is no evidence of invasion of the media in muscular or elastic arteries by the loose myxoid connective tissue of the intima, although the internal elastic membrane is frequently disrupted. The intima is often thickened circumferentially; however, the process is sharply delimited longitudinally. The endothelial lining is usually intact. Movat's pentachrome stain, X50.

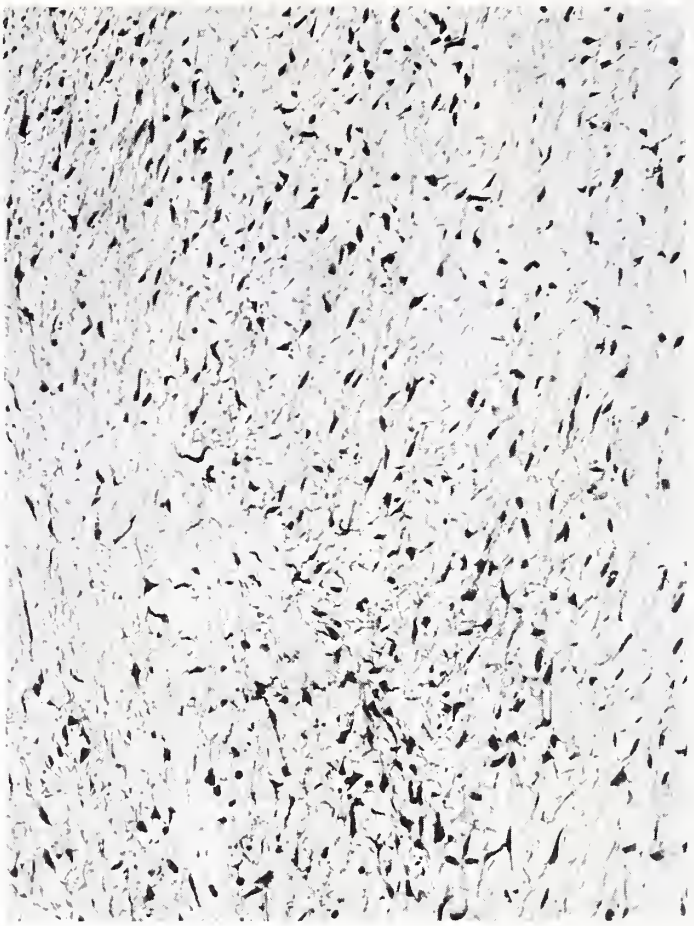


Figure 122
INTIMAL FIBROPLASIA OF THE AORTA
The thickened intima in figure 121 consists of spindle-shaped fibroblasts, often with considerable nuclear atypia set in acid mucopolysaccharide matrix. The tissue thickening the intima is highly cellular compared to the loose connective tissue normally found in the intima. At high magnification, it is remarkably similar to myxoid areas of myxoid fibrosarcoma. Movat's pentachrome stain, X90.

frequently extends for several centimeters, especially in large arteries. In the renal arteries, intimal fibroplasia is associated with focal arterial stenosis and poststenotic aneurysm formation. In arteries larger than the renals, this is seldom true; rather, there is diffuse arterial narrowing.

The loose fibromyxomatous intimal process and the circumscribed nature of the arterial involvement in intimal fibroplasia are reminiscent of sarcoma of the aorta that has been described as fibromyxosarcoma or intimal sarcoma (see figs. 120, 122). It has been reported that many of these tumors are confined to the aortic intima. We cannot definitely say that these are, in fact, examples of fibromuscular hyperplasia of the aorta, but we believe this must be part of the differential diagnosis of all so-called aortic intimal sarcomas or fibromyxosarcomas. This does not imply that fibrosarcoma of the aorta does not occur, because the lone aortic tumor in the AFIP collection is a fibrosarcoma with dis-

tant metastases and characteristic morphology and ultrastructure of a fibrosarcoma.

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Figure 123
INTIMAL FIBROPLASIA OF THE AORTA

Many of the fibroblasts within the thickened intima in figure 121 have abundant granular cytoplasm which is deeply eosinophilic. Ultrastructurally, the cytoplasm of these cells is filled with myofibrils and resembles smooth muscle cells, except for the absence of a well defined basement membrane. These cells are thought to represent transformed fibroblasts and are characteristic of fibromuscular dysplasia. Movat's pentachrome stain, X350.

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PROFESSIONAL NOTES AND FINDINGS