PRIMARY NEOPLASMS AND CYSTS OF THE MEDIASTINUM*

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WITHOUT DOUBT bronchogenic carcinoma is the most commonly encountered primary intrathoracic neoplasm. There is less certainty as to the relative frequency of the various tumors and cysts which have their origin in the mediastinum.

Heuer and Andrus in 1940 stated that the group designated as dermoids or teratomas are "by far the commonest tumors of the mediastinum."[16] In 1946 Blades found that neurogenic tumors, closely followed by bronchogenic cysts, were the most numerous types among the mediastinal tumors observed by the Army Thoracic Surgery Centers in the United States during World War II.[1] The following year Bradford, Mahon, and Grow reported the experience of the Fitzsimmons General Hospital where more pericardial cysts had been seen than any other type of mediastinal neoplasm.[4] In 1949 Brewer and Dolley discussed the diagnosis and treatment of tumors of the mediastinum; in their 44 cases the neurogenic tumors were most frequently observed.[6]

Since mediastinal tumors are relatively uncommon lesions, it is unlikely that their true incidence can be determined from the experience of any one clinic. It should be possible, however, to obtain a fairly accurate estimate of their frequency and distribution by a survey of histologically verified cases observed in a general hospital clinic over an extended period of time. This report is based on such a survey.

MATERIAL

During the period July, 1933, to July, 1951, 101 patients with primary tumors or cysts of the mediastinum have been observed at the Johns Hopkins Hospital. This number represents an incidence of one in approximately 3400 admissions. In each case the diagnosis was verified by histologic examination. Only patients with lesions which arose primarily in the mediastinum have been included in this study. Those instances in which the mediastinum was involved by direct extension or by metastasis from an extramediastinal source or as part of a generalized lymphoma have been excluded. In 90 patients the diagnosis was confirmed at operation and in the 11 others it was established at autopsy. Sixty-four of these patients were male and 37 were female. Their ages ranged from three weeks to 68 years, although the majority (77 per cent) were over 20 years of age. There were 90 white and 11 colored patients in the group. Both public ward and private patients are included in this survey. Approximately one-half of the operations were performed by Dr. W. F. Rienhoff, Jr. and Dr. Alfred Blalock, while the remainder were carried out by various members of the surgical staff of the Johns Hopkins Hospital, chiefly during the tenure of the surgical residency. A summary of pertinent data

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concerning these patients is presented as an appendix.

TUMORS OF NEURAL ORIGIN

In this series 20 patients had mediastinal tumors of neural origin; this constitutes the largest group of histogenetically related neoplasms in this study. All but one of these tumors originated in the posterior mediastinum, and five of the 20 tumors were malignant. Fifteen of the neurogenic tumors occurred in children and young adults. Cough and dyspnea were present in the majority of the patients, and only four asymptomatic neurogenic tumors were found on routine roentgenologic examination. The neurogenic tumors in this series have been classified as follows: ganglioneuroma, neurofibroma, neurinoma, neurogenic sarcoma, and neuroblastoma.

Ganglioneuroma and Ganglioneurosarcoma. These tumors, which arise from the sympathetic ganglia are most frequently observed along the great paravertebral chains, but in rare instances may arise from smaller sympathetic ganglia in a variety of locations. In Stout's study of the anatomical distribution of ganglioneuromas the mediastinum was found to be second to the abdomen as the most frequent site.[37] These tumors occur more commonly in childhood and adolescence than in later life.

In the present series ganglioneuroma occurred in six patients and ganglioneurosarcoma was found in one patient. The incidence of malignant change (14 per cent) in the ganglioneuromas of this series is in accord with the statistics compiled by Stout. Four patients were under 12 years of age. All the tumors arose in the posterior mediastinum. The six benign lesions were associated with minimal symptoms or none at all; the single malignant tumor, which at operation was found to have invaded the hilum of the lung and pericardium, was accompanied by intercostal pain, fever and loss of weight. The histologic appearance of a typical ganglioneuroma is seen in Figure 1.

Neurofibroma and Neurinoma. Neurofibromas are thought to arise from the peripheral or endoneural connective tissue and may be distinguished from the tumors of the sheath of Schwann or neurinomas, which are characterized histologically by elongated fusiform cells with palisading of the nuclei.[36] However, the gross appearance and clinical behavior of these two histologic types seem to be similar and for practical purposes they may be considered together.

In this series nine patients were found to have benign tumors of nerve sheath origin. In four cases the tumors were classified as neurofibromas and in five instances as neurinomas. Each of the nine tumors lay in the posterior mediastinum along the paravertebral gutter. In two cases there was an hourglass extension through an intervertebral foramen into the spinal canal with evidence of compression of the cord. In six instances the tumor originated from one of the upper intercostal nerves and in three cases it arose from a nerve in the midthoracic region. These observations are similar to those of Kent, Blades, Valle and Graham,[19] who point out that the appearance in a roentgenogram of a circumscribed nonpulsating, rounded mass in the posterior superior mediastinum should suggest the diagnosis of neurogenic tumor. Histologic characteristics of these tumors are seen in Figures 2 and 3.

Neurogenic Sarcoma. Malignant tumors of neural origin are much more commonly met with along the course of the peripheral nerves of the extremities than in the mediastinum.[36] Nevertheless, Kent and his associates[19] found that seven of 18 intrathoracic neurogenic tumors studied at the Barnes Hospital were malignant, and that 37 per cent of a collected series of 105 neurogenic tumors situated within the

thorax were considered malignant. Of the various types of malignant neurogenic tumors occurring in the mediastinum, neurogenic sarcoma is probably the commonest.[33] The exact histogenesis of this tumor remains obscure. Stewart and Copeland[36] support the earlier opinion of Verocay that most of these tumors arise from the Schwann cells; others have held that the connective tissue of the nerve sheath is the source of neurogenic sarcoma. Whatever the origin of this highly invasive tumor, it seems definite that neurofibromas and neurinomas of the mediastinum are capable of sarcomatous change and transformation into neurogenic sarcoma.

Two patients in the present series had primary mediastinal tumors which were classified as neurogenic sarcoma. In each instance the clinical manifestations suggested malignant disease. At operation each patient was found to have a very large invasive tumor, one of which arose posteriorly and the other anteriorly. Radical extirpation of the tumor and the left lung, which had been invaded, was attempted

FIG. 1 FIG. 2

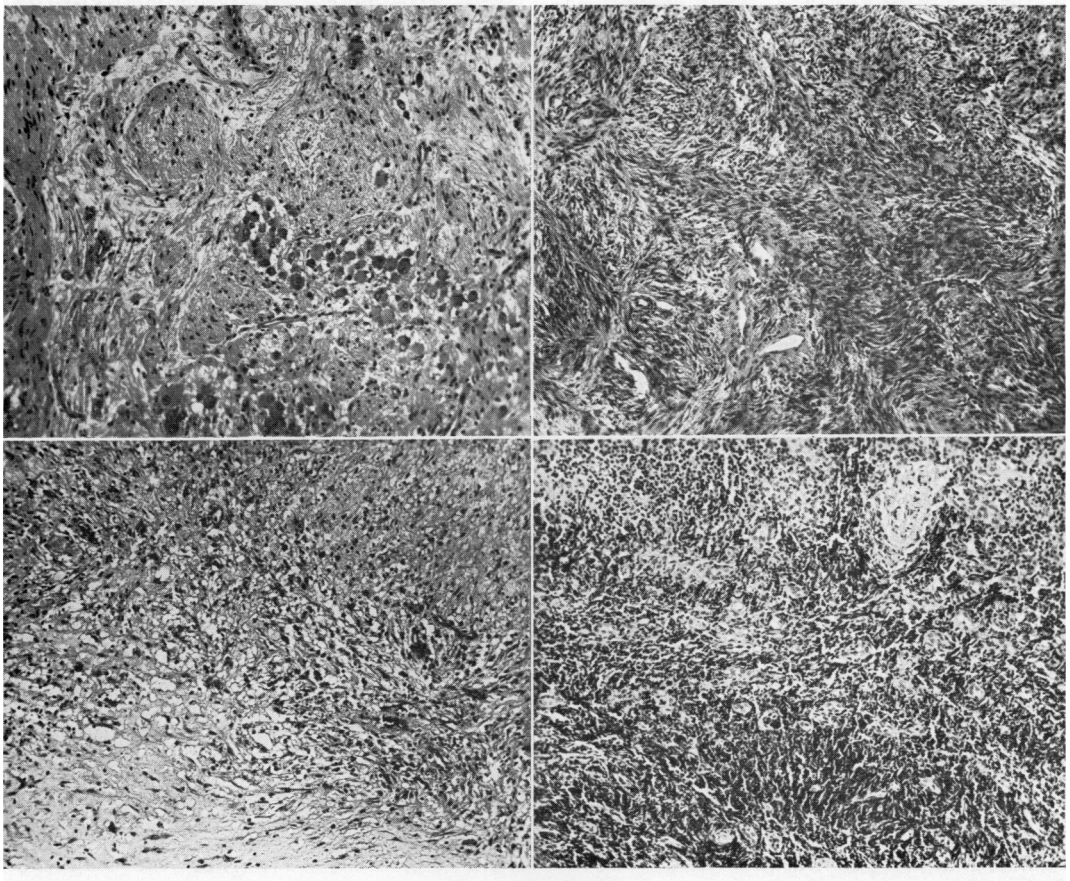
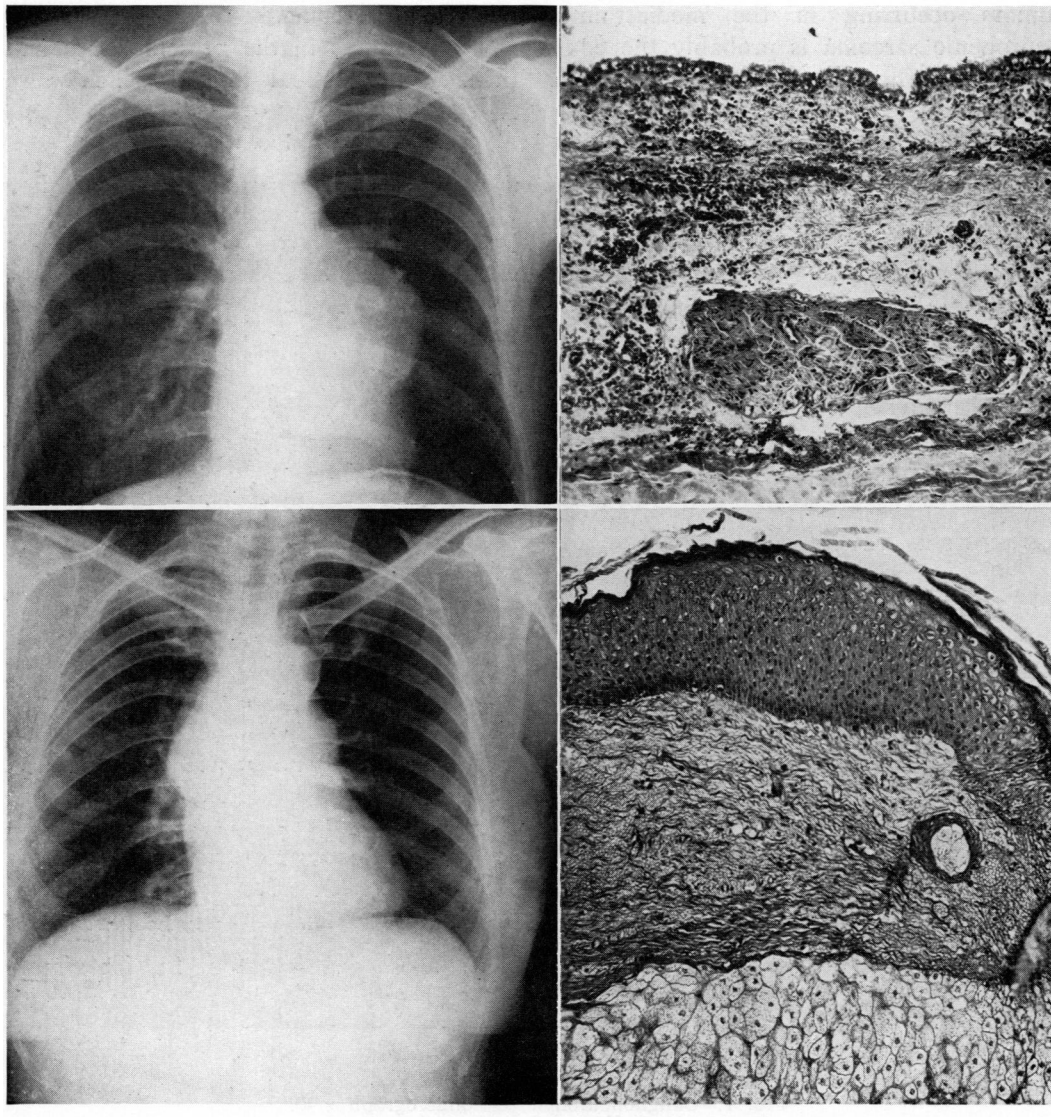


FIG. 3 FIG. 4

FIG. 1.—Ganglioneuroma: photomicrograph x 90.
FIG. 2.—Neurofibroma: photomicrograph x 90.
FIG. 3.—Neurinoma: photomicrograph x 90.
FIG. 4.—Neuroblastoma: photomicrograph x 90.

FIG. 5

A B



A B

FIG. 6

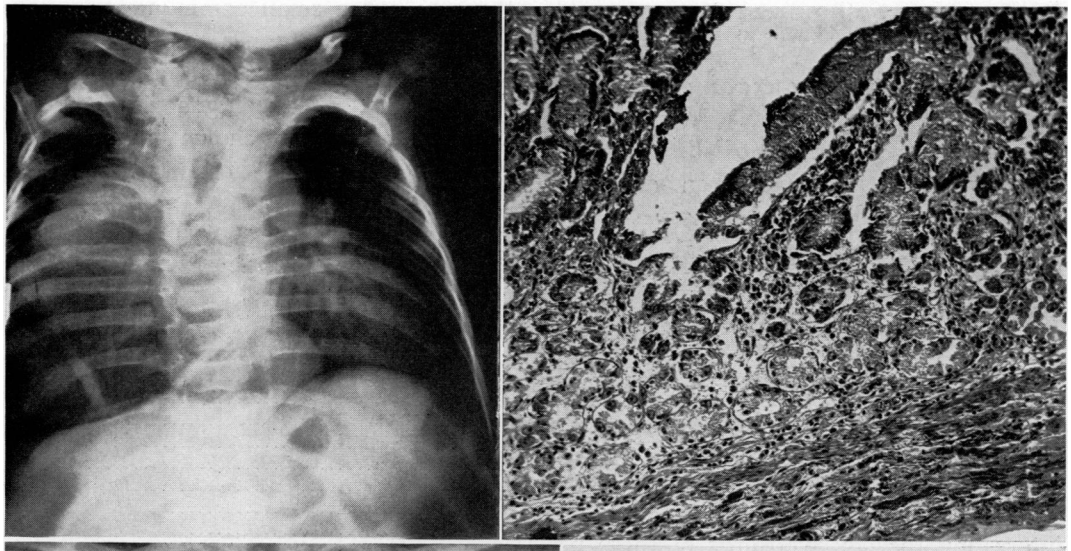
FIG. 5.—Bronchogenic cyst: P-A roentgenogram and photomicrograph x 100.
FIG. 6.—Dermoid cyst: P-A roentgenogram and photomicrograph x 100.

in one case, but this was followed by recurrence and death within a year.

Neuroblastoma. While neuroblastoma is most commonly seen as a retroperitoneal growth in young children, the tumor may arise from sympathetic tissue in many parts of the body in adult life as well as in childhood. This rapidly growing, highly invasive tumor arising primarily in the mediastinum was observed in two patients in the present series. One boy of six years was found to have a very large tumor

FIG. 7

A B



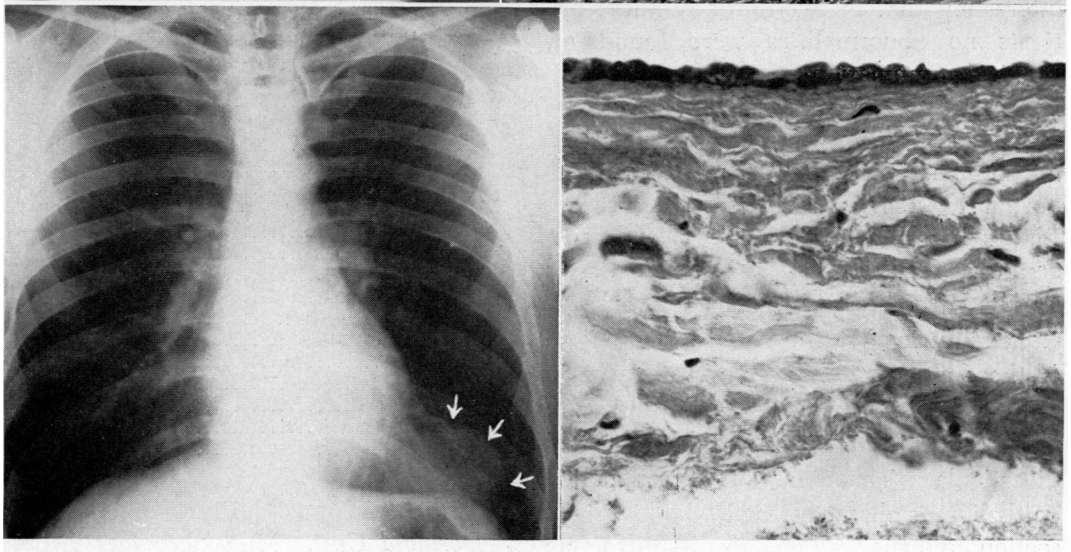


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FIG. 8

FIG. 7.—Enterogenous cyst: P-A roentgenogram and photomicrograph x 110.
FIG. 8.—Pericardial cyst: P-A roentgenogram and photomicrograph x 110.

which originated in the lower anterior mediastinum and projected into both right and left hemithoraces (Figure 4). In the other patient, a man of 47 years, the tumor lay in the posterior mediastinum and invaded the spinal canal with the production of cord compression. Although neither of these tumors could be completely removed, neuroblastoma is occasionally amenable to total surgical excision. Farber,[14] Ladd and Gross,[22] and others have pointed out that these highly malignant tumors, even when nonresectable, are not always fatal. In rare instances the rapidly growing tumor undergoes spontaneous necrosis and disappears, and even more rarely this malignant lesion

may "mature" into a benign ganglioneuroma.[11]

CYSTS

There are many types of cysts which occur in the mediastinum. In this series they comprise 17 per cent of all the lesions, and five varieties have been observed. These are classified as bronchogenic, dermoid, enterogenous, pericardial and nonspecific cysts. There were 17 patients, whose ages ranged from ten months to 68 years. Symptoms were present in all but four; in these the cysts were discovered on routine roentgenography of the chest. The majority of these lesions were in the anterior mediastinum (ten of 17) with the remainder in the posterior division. It is interesting that in two-thirds of these patients no abnormalities were found on physical examination.

Bronchogenic Cyst. In the literature reports of this type of cyst are relatively uncommon. Only 76 cases had been reported by 1947.[39] It is of interest that Blades found this to be the second most common mediastinal lesion in the cases reported from the Army Thoracic Surgery Centers during World War II.[1] The origin of these cysts is generally agreed to be in the tracheobronchial tree, and they are closely related to tracheal and bronchial diverticula. The ciliated pseudostratified epithelium is characteristic in the histologic section, and the wall contains fibrous tissue with or without cartilage and mucous glands.

In this series there were five bronchogenic cysts, four of which occurred in males. Three patients had chest pain and two had dyspnea and hemoptysis. While bronchogenic cysts may occur in any division of the mediastinum, they are usually centrally located in association with the major bronchi.[7] In this series, one projected into the anterior mediastinum, and four into the posterior division. The histologic sections showed ciliated, pseudostratified epithelium in each instance. In one case the cyst had a small communication with the lumen of the trachea, and possibly this lesion should be classified as a tracheal diverticulum. A roentgenogram and a photomicrograph are shown in Figure 5.

TABLE I.—*Primary Neoplasms and Cysts of the Mediastinum.*

Tumors of neural origin	20
Ganglioneuroma	6
Ganglioneuro-sarcoma	1
Neurinoma	5
Neurofibroma	4
Neurogenic sarcoma	2
Neuroblastoma	2
Thymoma	17
Benign	12
Malignant	5
Cysts	17
Bronchogenic	5
Dermoid	3
Enterogenous	2
Pericardial	2
Nonspecific	5
Carcinoma, undifferentiated, primary	10
Teratoma	9
Lymphosarcoma	6
Hodgkin's disease	5
Thyroid tumors	5
Adenoma	4
Carcinoma	1
Sarcoma	5
Spindle cell	3
Undifferentiated	2
Parathyroid adenoma	2
Lipoma	2
Fibroma	1
Leiomyoma	1
Mesothelioma	1
Total	101

Dermoid Cyst. Most observers include the teratomas with dermoid cysts. The reason for this association is their probable similarity of origin. Harrington introduced the term "teratoid" to be used collectively for these lesions.[15] In our opinion they present characteristics of pathology and behavior sufficiently different to require separate classification. A dermoid cyst contains only derivatives of skin and its appendages, whereas a teratoma contains derivatives of two or three germ layers. The histologic picture of the dermoid cyst usually shows

a lining of squamous epithelium and a fibrous tissue capsule with or without skin appendages. Hair and teeth are sometimes found in these cysts, and they are usually filled with sebaceous material. The incidence of malignancy is probably 13 per cent or less.[31] Virtually all are located in the anterior mediastinum.

There were three dermoid cysts in the present study. All occurred in females, although this is not a characteristic feature. One patient complained of pain and another of cough. The third cyst was found on routine roentgenography. All of the cysts occupied the anterior mediastinum and showed evidence of calcification. Typical roentgenographic and histologic pictures are seen in Figure 6.

FIG. 9

A B

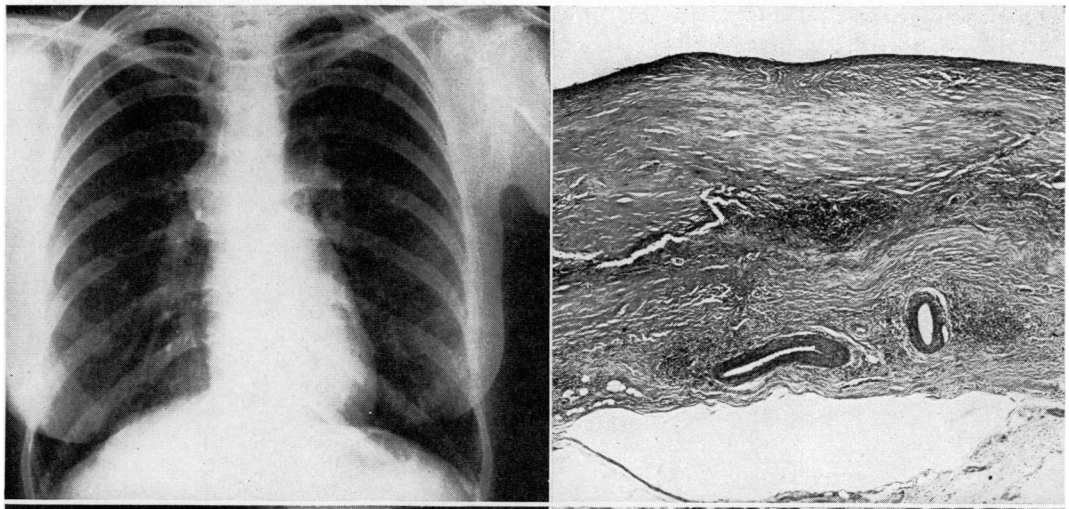

FIG. 10

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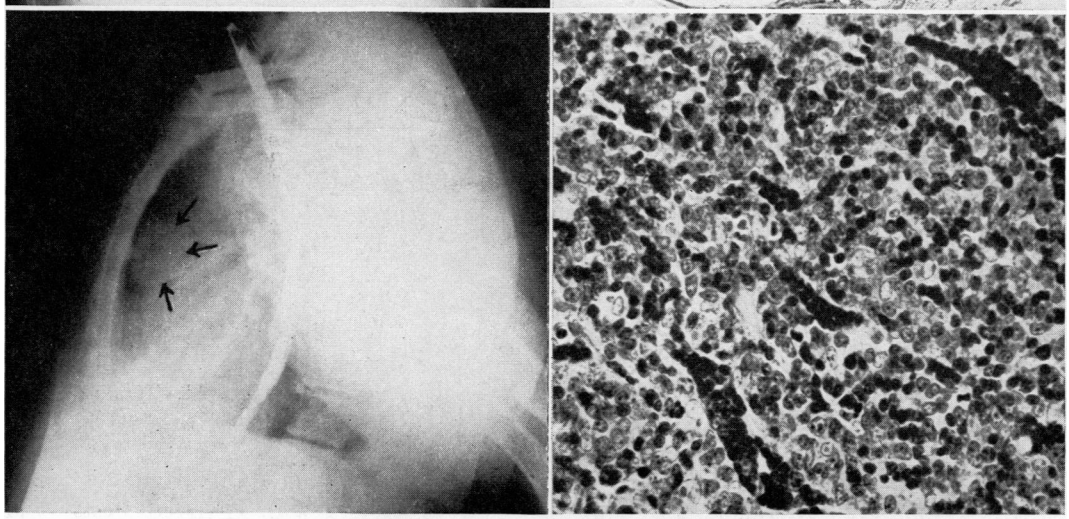


FIG. 9.—Nonspecific cyst: P-A roentgenogram and photomicrograph x 20.
FIG. 10.—Thymoma, benign: lateral roentgenogram and photomicrograph x 350.

Enterogenous Cyst. Mediastinal cysts of enteric origin are of relatively infrequent

FIG. 11

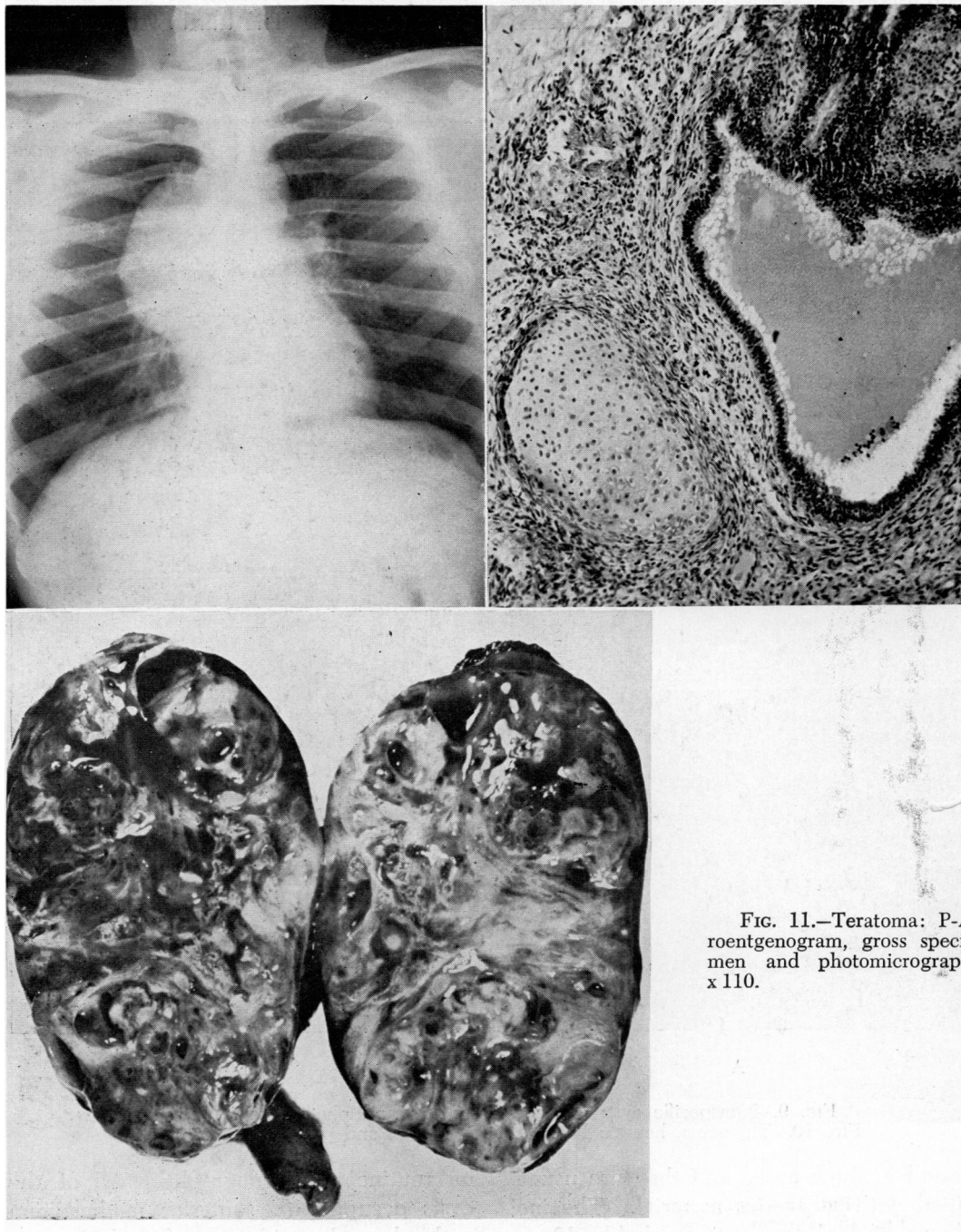


FIG. 11.—Teratoma: P-A roentgenogram, gross specimen and photomicrograph x 110.

occurrence. While they are certainly developmental anomalies, the exact mechanism is debatable. Keith, Bremer, and others believe that they are essentially esophageal duplications, representing a failure of coalescence of primitive alimentary vacuoles in

a transverse axis.[5, 18, 23] Over 70 cases have been reported,[27] but a much smaller number have been treated surgically. Enteric cysts are usually found at an early age, characteristically in infancy or early childhood. Virtually all of them occur in the posterior mediastinum, and it is interesting that the great majority occur on the right side. The symptoms are chiefly those of respiratory distress and may vary with the size of the lesion. The cysts may become quite large, and are filled with fluid which sometimes contains hydrochloric acid and gastric enzymes.[23, 34]

There were two such cysts in this series. These were discovered at the ages of two months and two years. The chief symptom in each patient was dyspnea. Both cysts were in the posterior mediastinum, one on the right side and the other projecting into both hemithoraces. Gastric mucosa was present in each cyst. A roentgenogram and a photomicrograph of one of these cysts are shown in Figure 7.

FIG. 12

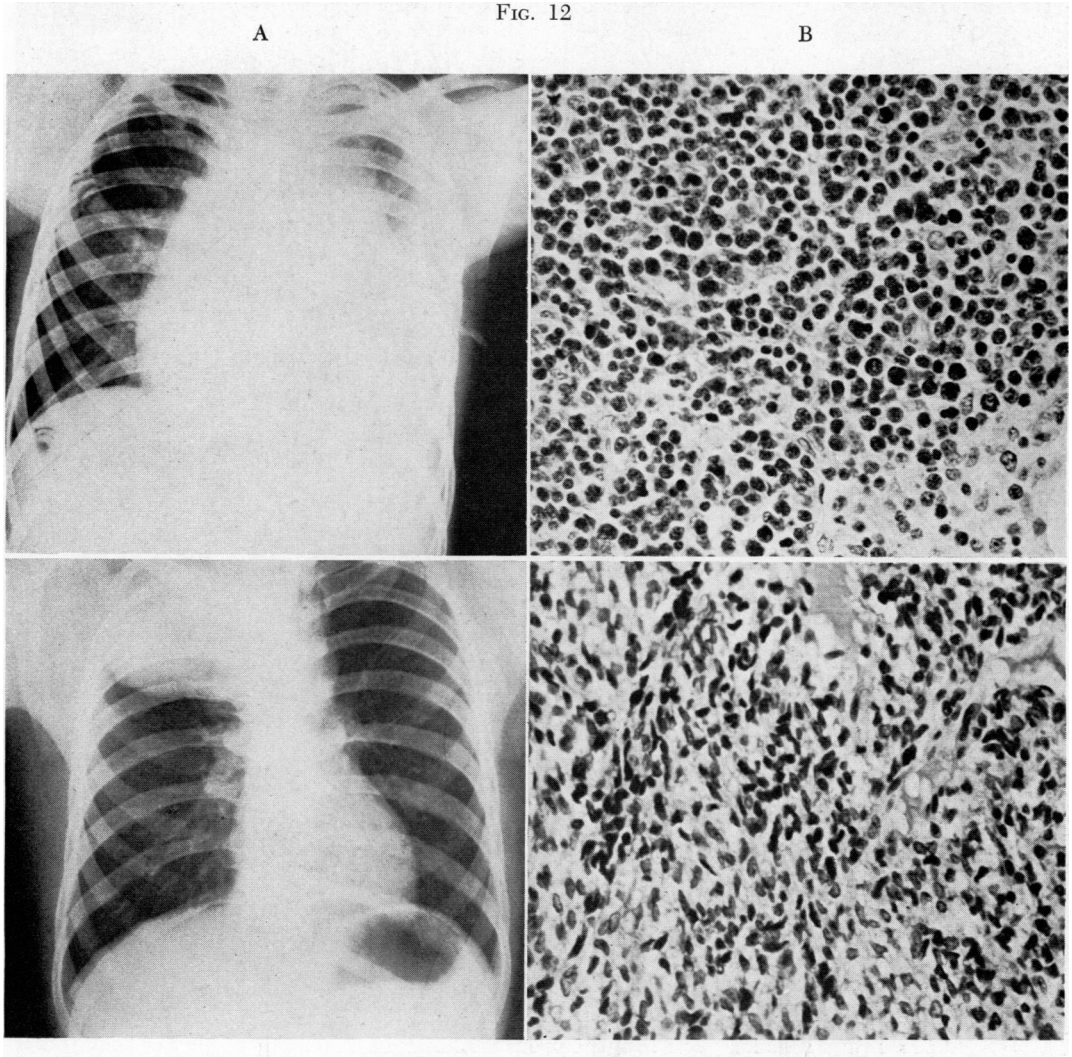
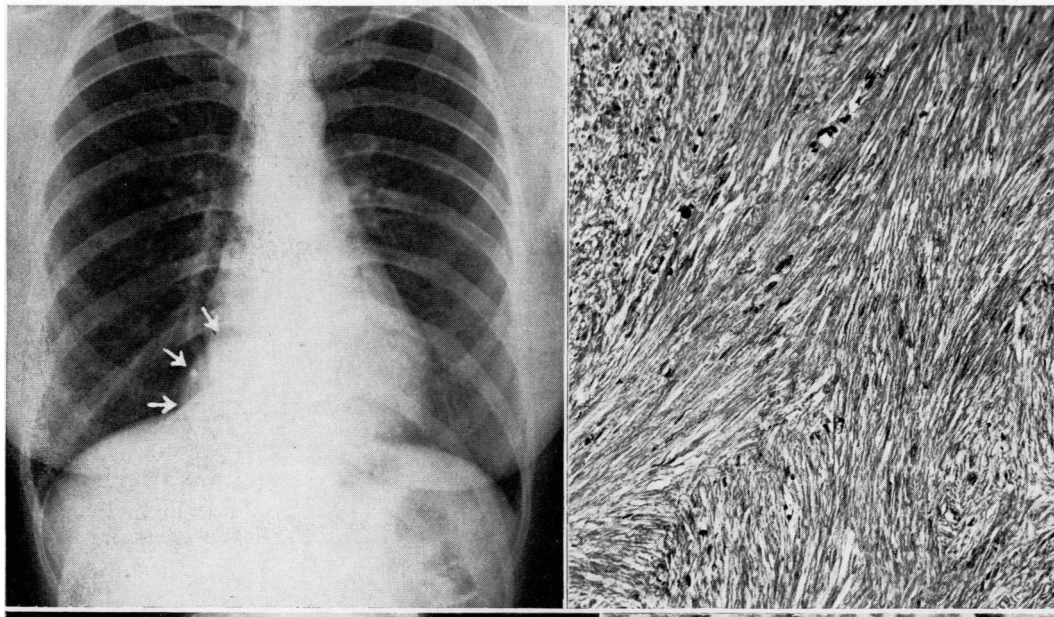


FIG. 13

FIG. 12.—Lymphosarcoma: P-A roentgenogram and photomicrograph x 340.
FIG. 13.—Sarcoma, spindle cell type: P-A roentgenogram and photomicrograph x 330.

FIG. 14



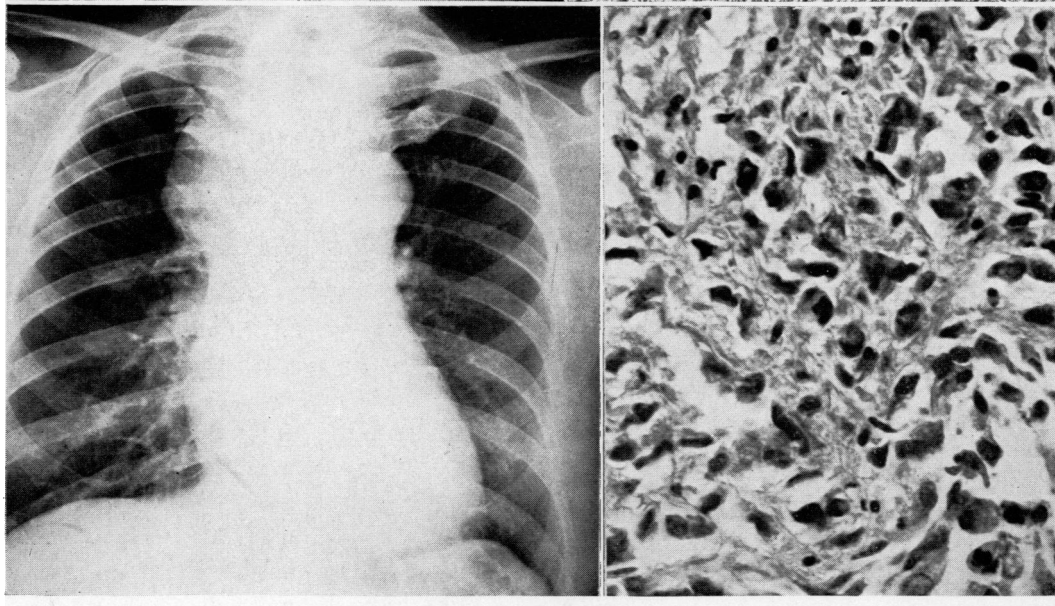


FIG. 15

FIG. 14.—Leiomyoma: P-A roentgenogram and photomicrograph x 125.
FIG. 15.—Mesothelioma: P-A roentgenogram and photomicrograph x 400.

Pericardial Cyst. Over 50 pericardial coelomic cysts are described in recent surgical reports.[13, 21, 24, 25, 29] There are at present two theories relative to the origin of these lesions. In 1940 Lambert reported two cases and expressed the opinion that

they resulted from the failure of the primitive pericardial lacunae to merge into a single cavity.[24] It is Kindred's belief that the cysts are a result of abnormal folds in the embyronic advance of the pleura, with the formation of saclike cysts which may project into either the pleural or the pericardial cavity.[20] The lesions are usually asymptomatic, being discovered in many instances on routine roentgen ray examination. The commonest sites are the cardiophrenic angles, especially the right. Grossly, the cysts have thin walls and contain watery, clear fluid; hence the term "spring-water cysts." In some instances there is a pericardial attachment, and cases with pericardial communications are described. Histologically their wall is fibrous and the lining is a single layer of mesothelial cells. They are always benign.

TABLE II.—*Clinical Manifestations in 60 Benign and 41 Malignant Primary Tumors and Cysts of the Mediastinum.*

	Benign (%)	Malignant (%)
Pain	34	58
Cough	18	50
Dyspnea	22	30
Hemoptysis	12	10
Dysphagia	7	15
Weight loss	5	37
Hoarseness	2	12
Abnormal physical findings	55	75

There were two such cysts in the present series. One was discovered on routine radiography of the chest ten years before the patient agreed to operation. During this interval he had complained of very slight discomfort in the chest. At operation a cyst was found at the left cardiophrenic angle (Figure 8). The chief symptom of the second patient was also pain in the chest. A sharply outlined mass at the right cardiophrenic angle was found on roentgenography.

Nonspecific Cyst. Although most of the cysts located in the mediastinum are histologically distinct, there are certain ones which defy a specific diagnosis. In the present study there were five patients who had primary mediastinal cysts which, on microscopic examination, showed only a fibrous tissue capsule with no epithelial or mesothelial lining. These patients ranged between the ages of 32 and 57 years. Four of the five patients had symptoms, chiefly pain. Only one showed any evidence of abnormality on physical examination. Four cysts were in the anterior mediastinum and one was in the posterior mediastinum. The cyst contents have varied from clear fluid to necrotic debris. There are several possible sources of these lesions. They may be dermoid cysts in which the epithelial lining is absent, or necrotic lymph nodes, or cysts of mesothelial or bronchial origin in which the lining is not demonstrable. A roentgenogram and photomicrograph are seen in Figure 9.

THYMOMA

The thymus is the source of a relatively large group of benign and malignant neoplasms. There are numerous surveys of these tumors in the literature, and no attempt will be made to give a detailed review of them.[2, 28, 35] The association of these lesions with myasthenia gravis has been given considerable attention in recent years, but this relationship continues to be a poorly understood one. The most frequent symptoms in patients subsequently shown to have a thymic neoplasm are those of myasthenia gravis. This is particularly true in those instances in which the tumor is benign. Pressure symptoms such as cough, dyspnea, and pain may be present with benign lesions but are much more common with the malignant ones. The location of these tumors is almost always in the anterior or superior mediastinum. Abnormal physical findings other than those of myasthenia gravis are not common. Nearly all thymic neoplasms are demonstrable by radiography.

The classification of thymic tumors has been a difficult problem, but there is a growing tendency to include the majority of these lesions under the term "thymoma."[35] In these tumors there are two primary cellular elements, those of epithelial and those of lymphocytic origin. The former are frequently designated reticular cells and the latter thymocytes. The proportions of these two cellular components may vary widely in individual tumors. As the tumor

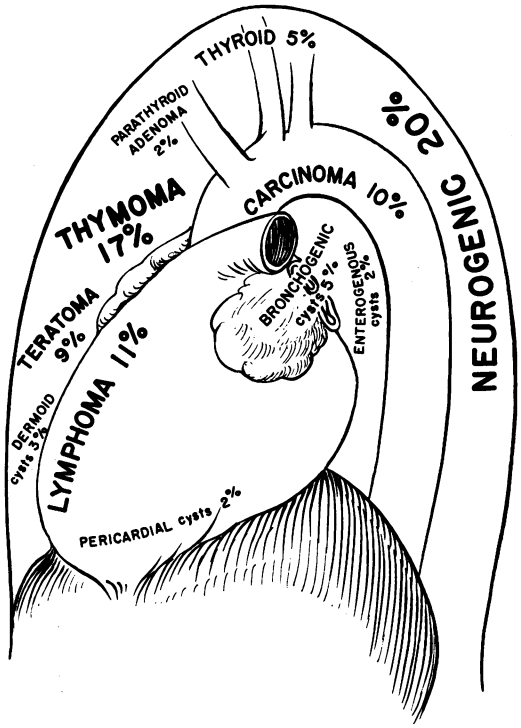


FIG. 16.—Diagram showing percentage distribution in this series and usual position of the commoner mediastinal tumors and cysts (after Brewer and Dolley[6]).

becomes more malignant, the cellular pattern becomes increasingly undifferentiated. The Symmers' classification of the malignant tumors is rather complex and has not been used in this study.[38]

Although many exceptions are now noted in the literature,[1, 26, 35] in general, benign thymic tumors are associated with myasthenia gravis whereas malignant ones are not. The statistics of the Mayo Clinic show that 15 per cent of patients with myasthenia gravis have thymic neoplasms and that 75 per cent of thymic neoplasms occur in patients with this disease.[35]

There were 17 patients with tumors of the thymus in the present survey. Ten of these occurred in males and seven in females, with an age distribution of 30 to 61 years. The average age for both sexes was 44. Twelve of the tumors were benign and five were malignant. Eight benign neoplasms occurred in patients with myasthenia gravis, and only two of these had a symptom—slight substernal pain—which was referable to the mass itself. In the malignant group four of the five patients had symptoms, and on physical examination all had abnormalities in the chest. Usually the symptoms were multiple, including cough, dyspnea, hoarseness, dysphagia, pain, and weight loss. Four of the five patients had demonstrable metastases. None had myasthenia gravis. Of the entire group of thymomas, ten were in the anterior mediastinum and the remainder in the anterior and the superior mediastinum. A roentgenogram and photomicrograph are seen in Figure 10.

UNDIFFERENTIATED CARCINOMA

In a study of mediastinal lesions there is a rather perplexing group which appears to be primary neoplasms and on histologic examination are found to be undifferentiated carcinoma. In this survey there were ten cases of this type. Those instances in which a primary lesion could be demonstrated in the lung or other organ, and cases in which the histologic pattern was sufficiently distinct to be of diagnostic value were not included. Only those patients in whom clinical investigation or autopsy failed to reveal any primary site other than the mediastinum were considered. In the series of Heuer and Andrus, 31 mediastinal carcinomas were shown to have originated in the lung, 12 were metastases from other sites, and 17 were considered to be pri-

mary mediastinal tumors.[16] In this group of cases, which are classified as primary carcinomas of the mediastinum, it is possible that an extramediastinal primary site existed and escaped detection. However, it is certainly possible for carcinoma to develop as a primary mediastinal lesion, for example, from the thymus, a dermoid cyst or a teratoma. In the absence of a demonstrable primary source elsewhere, this perplexing group of tumors can only be classified as primary mediastinal carcinoma.

Of the ten patients in this study with primary undifferentiated carcinoma of the mediastinum, nine were males. Although this incidence corresponds to that found in primary carcinoma of the lung, only one of these patients had hemoptysis. The average age was 45 years with a range of 24 to 59. Each of these tumors produced symptoms, chiefly pain, weight loss, cough, dyspnea, and hoarseness. Two patients had obstruction of the superior vena cava. Four tumors occurred in the anterior and four in the superior mediastinum. Two were in the posterior mediastinum. In no instance could origin in the lung be demonstrated. Histologic section showed undifferentiated carcinoma in each case.

TERATOMA

These interesting tumors are made up of derivatives of two or more germ layers in varying degrees of differentiation and histologic organization. They almost invariably lie in the anterior mediastinum and frequently form large globular masses which may project into both hemithoraces. Their relation to the dermoid cysts has formed the basis for the use of such terms in classification as "teratoid" and "teratodermoid." Grossly, the teratomas are usually solid tumors, but they may occur as multiloculated cystic masses or as large monocystic lesions in whose wall elements of two or more primitive tissues are found. Like teratomas elsewhere in the body, those in the mediastinum have a rather high potential for malignant change. Their clinical characteristics have been fully discussed by Harrington[15] and by Rusby.[31]

All of the nine teratomas in this series arose in the anterior mediastinum. Eight of the nine tumors occurred in males, and with a single exception the patients were children or young adults. All of the tumors were of great size and none was asymptomatic. Four of the nine proved to be malignant. Radiologic, gross and histologic features of one of these tumors are seen in Figure 11.

TABLE III.—*Position of Lesion in Mediastinum in 101 Cases.*

Anterior	46
Posterior	36
Superior	7
Anterior-superior	12

LYMPHOSARCOMA

The lymphoid tissue of the mediastinum is commonly involved secondarily by the various manifestations of the so-called malignant lymphomata. Not infrequently lymphosarcoma originates in the mediastinum as a primary neoplasm and must be considered as one of the commonest of the malignant tumors which arise in this region.[16] According to Schafer[33] and others, the mediastinal nodes are secondary only to the cervical nodes in the frequency with which they are the site of origin of lymphosarcoma. In the mediastinum this tumor most frequently has an anterior position. In addition, the hilar nodes on one or both sides are commonly involved, with the production of the rather characteristic radiologic appearance of a mass with a scalloped outer margin located anteriorly and centrally in the mediastinum.

In the present survey six patients with primary mediastinal lymphosarcoma were studied. The tumor arose anteriorly in four instances and posteriorly in two others. In only one case was the tumor sufficiently well localized to permit excision. This pa-

tient has survived for six years with no evidence of recurrence. A roentgenogram and a photomicrograph are seen in Figure 12.

HODGKIN'S DISEASE

When Hodgkin's disease involves the mediastinal nodes there are usually coexisting manifestations in the lymphoid tissue elsewhere in the body.[17] Rarely, however, Hodgkin's disease makes its first clinical appearance as a tumor of the mediastinum, and early in its course there may be no detectable clinical evidence of other lesions. We have chosen arbitrarily to include Hodgkin's disease in this survey of primary mediastinal tumors despite the fact that there is some question whether this disease is a true neoplasm.

In this study there were five patients who presented originally the clinical and radiologic manifestations of mediastinal tumor and in whom a diagnosis of Hodgkin's disease was ultimately established by mediastinal exploration and biopsy of the tumor. In all of the five patients included in the present study the mass presented primarily in the anterior mediastinum. None of these patients showed clinical evidence of involvement of the lymphatic system elsewhere concomitant with the manifestations of mediastinal tumor. The tumor could be grossly removed in only one patient.

INTRATHORACIC THYROID TUMORS

Intrathoracic goiter is relatively rare in this country. In a series of 11,800 thyroidectomies at the Cleveland Clinic only 97 goiters (less than one per cent) were intrathoracic.[10] The careful anatomical study of Wakely and Mulvany showed that in 111 of their series of 1265 thyroidectomies some portion of the goiter was retrosternal.[41] Of these, only 17 showed the major portion below the level of the thoracic inlet, and only three were totally intrathoracic (0.24 per cent). The diagnosis of the partially intrathoracic lesion is usually not difficult, since there is a concomitant cervical enlargement. The goiter, which is totally within the chest, however, has few definite characteristics. These patients may be divided into three clinical groups. There are those who have chiefly obstructive symptoms, such as dyspnea, dysphagia and hoarseness. Others have the manifestations of hyperthyroidism. A third group consists of those patients in whom the goiter is asymptomatic and is found on routine roentgenography. Fluoroscopy may aid in differential diagnosis, as intrathoracic goiter may rise with swallowing, since there is usually a vascular or other connection with the cervical thyroid. Recently, radioactive iodine has been used successfully in the diagnosis of intrathoracic goiter.[40] The majority of these lesions are benign adenomas.

In this series there were five patients who had thyroid lesions which were completely intrathoracic. Four goiters were associated with pain, cough, or dyspnea, and the fifth was found on routine roentgenography. Four of the five patients were males, and the average age was 53 years. Histologic examination of these goiters showed benign adenoma in three cases, hyperplasia in another, and carcinoma in another.

SARCOMA

The sarcomas of the mediastinum form a heterogenous group of malignant tumors. They may arise from the connective tissue elements of any of the mediastinal structures or from pre-existing benign neoplasms in this region.[16] Fortunately, they are relatively rare tumors. With few exceptions, such as the sarcomas of neural, lymphatic or cartilaginous origin, they tend to be so undifferentiated as to make it difficult to identify the original cell type.

Five patients in this survey had poorly differentiated sarcomas which, as far as could be determined, arose primarily in the mediastinum. All were young or middle-aged adults and all had clinical manifestations of thoracic disease. The tumor occupied the anterior mediastinum in three patients, the posterior mediastinum in another, and the superior mediastinum in another. When exposed surgically, four of the sarcomas were found to be widely invasive and were not resectable. In the fifth case the tumor was grossly well encapsulated and could be removed. Histologically, three of these tumors were classified as undifferentiated sarcomas while two were sarcomas of the spindle cell type. Radiologic and histologic characteristics of one of these tumors are seen in Figure 13.

PARATHYROID ADENOMA

The fact that adenomas of the parathyroid gland may occur in the mediastinum is well known. It has been postulated that their presence in this position can be accounted for either by embryologic descent with the thymus or by displacement from the neck.[9] The theory of displacement is substantiated by the fact that adenomas in the posterior mediastinum have vascular pedicles from the neck. Those in the anterior mediastinum, which can arise there embryologically, derive their vascular supply locally. In 1947 Thompson listed 19 cases of mediastinal parathyroid adenoma in a collective review.[39] Parathyroid adenomas in any location are nearly always benign, and this is equally true of those that occur in the mediastinum. Histologically, the adenomas are composed of several different cellular types. The chief cells, pale and dark oxphil cells, and clear cells are all usually present but in varying ratios. There has been an attempt to associate the chief cellular type with the activity of the lesions, but this point remains unsettled.

In the present series there have been two such adenomas, both in the superior mediastinum. These have been previously reported by Dr. William F. Rienhoff, Jr.[30] These patients had renal calculi and were found also to have elevated blood calcium and reduced phosphorus levels. In each case the thyroid region was first explored and found to be negative; the mediastinum was then explored through a median sternotomy and the adenoma found.

LIPOMA, FIBROMA, LEIOMYOMA AND MESOTHELIOMA

The more unusual types of mediastinal tumors merit only brief mention. The individual cases are recorded in the appendix. In 1940 Heuer and Andrus were able to collect 42 mediastinal lipomas and added a case of their own.[16] Some of these were dumb-bell tumors, with one component portion in the thoracic wall. In the present survey two lipomas were encountered: one in a child of eight in whom the lesion was found on routine radiography of the chest, and another in a woman of 53 who complained of pain in the chest. Both tumors were in the posterior mediastinum.

Fibromas also are unusual in the mediastinum. In 1940, 32 were recorded in the literature; others have since been reported.[8] One of the patients in the present study, a 14-year-old girl, had hoarseness and a left Horner's syndrome. The roentgenogram showed a mass in the upper posterior mediastinum projecting into the left hemithorax. At operation a benign fibroma was found and excised.

Leiomyoma arising from the esophageal wall and projecting into the mediastinum is an uncommon lesion. In 1950, Daniel collected from the literature 92 cases of leiomyoma of the esophagus.[12] The majority of these tumors were asymptomatic and only eight patients had been submitted to operation. In the present group one leiomyoma was observed in a woman

TABLE IV.—*Appendix.*

No.	Age	Sex	Duration of Symptoms	Found on Routine Roentgenogram	Mass on Roentgenogram	Site of Origin in Mediastinum	Operation	Pathologic Diagnosis	Course
1	25	M	.....	+	Rt. lower chest	P	1936. Thoracotomy, mass excised	Ganglioneuroma	Well 1951
2	51	M	.....	..	Negative	P	1940. Autopsy	Ganglioneuroma	Died
3	3	M	1 yr.	..	Rt. upper chest	P	1942. Thoracotomy, mass excised	Ganglioneuroma	Well 1951
4	18	M	.....	+	Rt. lower chest	P	1943. Thoracotomy, mass excised	Ganglioneuroma	Well 1951
5	12	M	1 yr.	..	Lt. hilus	P	1946. Thoracotomy, biopsy	Ganglioneuro-sarcoma	Died 1949
6	7	M	6 yr.	..	Rt. entire chest	P	1948. Thoracotomy, biopsy	Ganglioneuroma	Died during operation
7	6	M	1 yr.	..	Rt. apex	P	1949. Thoracotomy, mass excised	Ganglioneuroma	Well 1951
8	25	M	10 mo.	..	Lt. apex	P	1938. Thoracotomy, mass excised	Neurinoma	Well 1951
9	39	M	1 yr.	..	Lt. mid. chest	P	1941. Thoracotomy, mass excised	Neurinoma	Died after operation
10	25	M	.....	+	Rt. upper chest	P	1945. Thoracotomy, mass excised	Neurinoma	Well 1951
11	57	F	3 mo.	..	Lt. mid. chest	P	1947. Thoracotomy, mass excised	Neurinoma	Well 1951
12	1	F	2½ mo.	..	Rt. upper chest	P	1950. Thoracotomy, mass excised	Neurinoma	Alive 1951 (paraplegia)
13	45	F	9 mo.	..	Rt. upper chest	P	1934. Thoracotomy, mass excised	Neurofibroma	Disch. well. No follow-up
14	13	F	4 wk.	..	Rt. apex	P	1934. Thoracotomy, partial excision	Neurofibroma	Well 1935. No follow-up
15	27	F	1 mo.	..	Rt. mid. chest	P	1945. Thoracotomy, mass excised	Neurofibroma	Well 1951
16	52	M	.....	+	Rt. upper chest	P	1945. Thoracotomy, mass excised	Neurofibroma	Well 1951
17	24	M	13 yr.	..	Lt. entire chest	P	1944. Thoracotomy, mass excised	Neurogenic sarcoma	Died 1945 (recurrence)
18	50	F	8 mo.	..	Lt. upper chest	P	1946. Thoracotomy, biopsy	Neurogenic sarcoma	Died after operation
19	47	M	5 wk.	..	Mid. mediastinum	P	1938. Thoracotomy, biopsy	Neuroblastoma	Died 2 months later
20	6	M	3 wk.	..	Rt. lower chest	A	1948. Thoracotomy, biopsy	Neuroblastoma	Generalized metastases '48
21	32	F	3 yr.	..	Rt. upper chest	P	1941. Thoracotomy, mass excised	Bronchial cyst	Well 1951
22	24	M	3 yr.	..	Rt. ant. mediastinum	A	1944. Thoracotomy, mass excised	Bronchial cyst	No follow-up
23	27	M	5 yr.	..	Upper post. mediastinum	P	1944. Sternotomy, mass excised	Bronchial cyst	Well 1951
24	31	M	3 yr.	..	Lt. hilus	P	1948. Thoracotomy, mass excised	Bronchial cyst	Died during operation
25	65	M	.....	+	Lt. post. mediastinum	P	1951. Thoracotomy, mass excised	Bronchial cyst	Well 1951
26	50	F	.....	+	Ant. mediastinum	A	1936. Thoracotomy, mass excised	Dermoid cyst	Well 1951
27	18	F	9 mo.	..	Lt. hilus	A	1944. Thoracotomy, mass excised	Dermoid cyst	Well 1951
28	50	F	5 yr.	..	Rt. hilus	A	1948. Sternotomy, mass excised	Dermoid cyst	Well 1951
29	68	M	7 wk.		Rt. cardiophrenic angle	A	1948. Thoracotomy, mass excised	Pericardial cyst	Well 1951
30	32	M	.....	+	Lt. cardiophrenic angle	A	1950. Thoracotomy, mass excised	Pericardial cyst	Well 1951
31	2 mos.	F	1 wk.	..	Rt. entire chest	P	1941. Autopsy	Enteric cyst (gastric mucosa)	Dead on arrival
32	2	M	2 wk.	..	Rt. and lt. post. mediastinum	P	1947. Thoracotomy, cyst marsupialized	Enteric cyst (gastric mucosa)	Died after operation
33	32	F	4 yr.	..	Mid. mediastinum	P	1936. Thoracotomy, mass excised	Non-specific cyst	Well 1951
34	33	M	7 yr.	..	Rt. lower mediastinum	A	1943. Thoracotomy, mass excised	Non-specific cyst	Disch. well. No follow-up
35	45	F	.....	+	Rt. hilus	A	1948. Thoracotomy, mass excised	Non-specific cyst	Well 1951
36	43	F	1½ yr.	..	Upper mediastinum	A	1949. Thoracotomy, mass excised	Non-specific cyst	Well 1951
37	57	M	1 yr.	..	Rt. mid. mediastinum	A	1951. Thoracotomy, mass excised	Non-specific cyst	Well 1951
38	36	F	4 yr.	..	Ant. mediastinum	A	1933. Autopsy	Thymoma	Died
39	38	M	1 yr.	..	Sup. mediastinum	A	1933. Sternotomy, mass excised	Thymoma	Alive 1951 (myasthenia)
40	50	F	1 mo.	..	Rt. ant. mediastinum	A	1942. Thoracotomy, mass excised	Thymoma	Died p.o. (miliary tbc.)
41	48	F	7 mo.	..	Rt. mid. mediastinum	A	1943. Sternotomy, mass excised	Thymoma	Died 1946 (myasthenia)

TABLE IV.—(*Continued*).

No.	Age	Sex	Duration of Symptoms	Found on Routine Roentgenogram	Mass on Roentgenogram	Site of Origin in Mediastinum	Operation	Pathologic Diagnosis	Course
42	47	M	3 yr.	..	Lt. ant. mediastinum	A	1944. Sternotomy, mass excised	Thymoma	Died 1945 (myasthenia)
43	43	F	3 mo.	..	Ant.-sup. mediastinum	A-S	1945. Sternotomy, mass excised	Thymoma	Died 1945 (myasthenia)
44	44	M	6 mo.	..	Negative mediastinum	A-S	1947. Sternotomy, mass excised	Thymoma	Died 1947 (myasthenia)
45	43	F	1 yr.	..	Ant.-sup. mediastinum	A-S	1947. Sternotomy, mass excised	Thymoma	Died 1947 (myasthenia)
46	51	F	1½ yr.	..	Ant. mediastinum	A	1948. Sternotomy, mass excised	Thymoma	Died 1951 (myasthenia)
47	57	F	.....	+	Rt. apex	A	1949. Thoracotomy, mass excised	Thymoma	Well 1950
48	35	M	2 yr.	..	Ant.-sup. mediastinum	A-S	1944. Sternotomy, mass excised	Thymoma	Well 1951 (myasthenia)
49	39	M	.....	..	"Enlarged pulmonary conus"	A	1944. Autopsy	Thymic cyst	Died (Banti's disease)
50	30	M	3 wk.	..	Lt. hilus	A-S	1934. Autopsy	Carcinoma of thymus	Died
51	61	M	1½ yr.	..	Sup. mediastinum	A-S	1937. Autopsy	Carcinoma of thymus	Died
52	53	M	5 mo.	..	Rt. apex	A-S	1942. Autopsy	Carcinoma of thymus	Died
53	48	M	.....	..	Lt. upper chest	A	1942. Autopsy	Carcinoma of thymus	Died
54	40	M	.....	+	Lt. upper chest	A	1950. Thoracotomy, biopsy	Carcinoma of thymus	Died 1951
55	24	M	1 yr.	..	Lt. hilus	A	1938. Thoracotomy, mass excised	Carcinoma	Disch. alive. No follow-up
56	56	M	6 wk.	..	Lt. hilus	P	1941. Thoracotomy, biopsy	Carcinoma	Disch. alive. No follow-up
57	54	M	3 mo.	..	Post. mediastinum	P	1943. Thoracotomy, biopsy	Carcinoma	Died after operation
58	26	F	2 wk.	..	Lt. hilus	A	1943. Sternotomy, biopsy	Carcinoma	Died 1944
59	28	M	2 mo.	..	Retromanubrial	S	1944. Sternotomy, biopsy	Carcinoma	Died 1944
60	46	M	6 mo.	..	Rt. upper chest	S	1945. Sternotomy, biopsy	Carcinoma	Died after operation
61	41	M	3 yr.	..	Lt. upper chest	A	1946. Thoracotomy, biopsy	Carcinoma	Died 1947
62	50	M	2 yr.	..	Rt. upper chest	A-S	1947. Thoracotomy, biopsy	Carcinoma	Died 1947
63	59	M	2 yr.	..	Ant. mediastinum	A	1950. Thoracotomy, biopsy	Carcinoma	Died after operation
64	58	M	5 mo.	..	Sup. mediastinum	S	1950. Sternotomy, biopsy	Carcinoma	Died 4 mo. p.o.
65	32	M	2 mo.	..	Ant. mediastinum	A	1935. Thoracotomy, mass excised	Teratoma	Died after operation
66	49	M	1 mo.	..	Rt. entire chest	A	1938. Thoracotomy, mass excised	Teratoma	Died 1939 (metastases)
67	19	M	5 mo.	..	Rt. hilus	A	1940. Thoracotomy, mass excised	Teratoma	Well 1951
68	1	F	.....	..	Rt. hilus	A	1947. Autopsy	Teratoma	Died
69	33	M	3 mo.	..	Rt. lower chest	A	1941. Thoracotomy, mass excised	Teratoma	Well 1951
70	32	M	1 yr.	..	Lt. chest	A	1943. Thoracotomy, mass excised	Teratoma	Died 5 mo. p.o. operation (metastases)
71	17	M	6 mo.	..	Rt. mid. chest	A	1949. Thoracotomy, mass excised	Teratoma	Well 1951
72	12	M	14 mo.	..	Rt. entire chest	A	1950. Thoracotomy, mass excised	Teratoma	Died after operation
73	15	M	6 mo.	..	Rt. entire chest	A	1951. Thoracotomy, mass excised	Teratoma	Well 1951
74	20	M	2 wk.	..	Rt. mediastinum	A	1941. Thoracotomy, biopsy	Lympho-sarcoma	Died during operation
75	18	F	.....	+	Lt. post. chest	P	1945. Thoracotomy, mass excised	Lympho-sarcoma	Well 1951
76	49	M	.....	..	Lt. ant. chest	A	1946. Thoracotomy, mass excised	Lympho-sarcoma	Died 1950 (recurrence)
77	8	M	2 wk.	..	Lt. upper chest	A	1947. Thoracotomy, biopsy	Lymphosarcoma	Died 1947 (metastases)

TABLE IV.—(*Continued*).

No.	Age	Sex	Duration of Symptoms	Found on Routine Roentgenogram	Mass on Roentgenogram	Site of Origin in Mediastinum	Operation	Pathologic Diagnosis	Course
78	52	M	18 mo.	..	Rt. hilus	A	1944. Autopsy	Lymphosarcoma	Died
79	49	F	2 mo.	..	Rt. hilus	P	1947. Autopsy	Lymphosarcoma (reticulum cell)	Died
80	41	F	3 yr.	..	Retromanubrial	A	1944. Thoracotomy, mass excised	Hodgkin's disease	Alive 1951 (recurrence)
81	30	F	.....	..	Rt. hilus	A	1945. Thoracotomy, biopsy	Hodgkin's disease	Died 1946
82	33	F	2 yr.	..	Sup. mediastinum	A-S	1947. Thoracotomy, biopsy	Hodgkin's diease	Died after operation
83	56	F	3 wk.	..	Ant. mediastinum	A	1950. Thoracotomy, biopsy	Hodgkin's disease	Alive 1951
84	36	F	7 mo.	..	Rt. upper mediastinum	A-S	1951. Thoracotomy, biopsy	Hodgkin's disease	Alive 1951
85	38	F	6 yr.	..	Lt. upper mediastinum	A	1946. Thoracotomy, mass excised	Thyroid adenoma	Disch. well. No follow-up
86	61	M	18 yr.	..	Retromanubrial	A-S	1947. Excision of mass	Thyroid adenoma	Well 1950
87	57	M	6 mo.	..	Rt. hilus	P	1947. Sternotomy, mass excised	Thyroid adenoma	Well 1951
88	50	M	.....	+	Mid. post. mediastinum	P	1950. Thoracotomy, mass excised	Thyroid adenoma	Well 1951
89	57	M	5 yr.	..	Sup. mediastinum	S	1951. Thoracotomy, mass excised	Carcinoma of thyroid	Disch. alive
90	47	M	1½ yr.	..	Rt. upper mediastinum	A	1936. Thoracotomy, biopsy	Sarcoma	Died 1938
91	15	M	2½ yr.	..	Rt. upper chest	A-S	1947. Thoracotomy, biopsy	Sarcoma	Disch. alive. No follow-up
92	39	F	4 mo.	..	Both hemithoraces	A	1949. Thoracotomy, mass excised	Sarcoma	Alive 1951
93	48	M	4 mo.	..	Lt. lower chest	A	1941. Thoracotomy, biopsy	Spindle cell sarcoma	Died after operation
94	16	M	6 mo.	..	Rt. upper chest	P	1947. Thoracotomy, mass excised	Spindle cell sarcoma	Alive 1951 (metastases)
95	44	M	4 yr.	..	Negative	S	1944. Sternotomy, adenoma excised	Parathyroid adenoma	Well 1949
96	63	F	8 yr.	..	Negative	S	1945. Sternotomy, adenoma excised	Parathyroid adenoma	Died 1950 (uremia)
97	53	F	3 mo.	..	Rt. post. mediastinum	P	1939. Thoracotomy, mass excised	Lipoma	Died after operation
98	8	F	.....	+	Lt. post. mediastinum	P	1944. Thoracotomy, mass excised	Lipoma	Disch. well. No follow-up
99	14	F	5 yr.	..	Rt. post. mediastinum	P	1938. Thoracotomy, mass excised	Fibroma	Well 1951
100	31	F	.....	+	Post. mediastinum	P	1950. Thoracotomy, mass excised	Leiomyoma	Well 1951
101	58	M	3 mo.	..	Rt. upper chest	S	1951. Sternotomy, biopsy	Mesothelioma	Died after operation

of 31 years. The tumor was discovered on routine radiography. The roentgenogram showed an ovoid mass behind the heart, anterior to the lower thoracic vertebrae and projecting to the right of the midline. At operation a tumor 8 cm. in diameter, which arose from the muscular wall of the esophagus, was excised (Fig. 14).

Mesothelioma of the pleura is a well-recognized but rare lesion. One such tumor which arose from the mediastinal pleura was encountered in the present study. The patient had hoarseness, dysphagia, pain, and weight loss of three months' duration. A large, fairly well circumscribed, calcified mass which occupied the superior mediastinum and projected to the right was demonstrated by the roentgenogram. This particular lesion represents the type of mesothelioma which spreads rapidly and has both a carcinomatous and a fibrosarcomatous appearance, in contrast to the localized fibrosarco-

matous type. These differences have been emphasized recently.[32] A photograph of this patient's chest film and a photomicrograph of the tumor are shown in Figure 15.

DISCUSSION

The frequency and distribution of the various primary tumors and cysts of the mediastinum in patients observed during the last 18 years at the Johns Hopkins Hospital are indicated in Table I. It should be repeated that only histologically verified neoplasms and cysts of primary mediastinal origin were included in this survey, and that tumors which involved the mediastinum secondarily by direct extension or by metastases from extramediastinal sources were not considered. Since these data are based on the patient population of a general hospital clinic with no selectivity as to age or sex, they should afford a fairly accurate estimate of the true frequency and distribution of these tumors in the population as a whole.

Of the 101 primary mediastinal tumors, 60 were benign and 41 were malignant. As seen in Table I, tumors of neural origin were most frequently encountered, followed by thymomas and the various types of cysts. Neurogenic tumors were the most numerous of the primary mediastinal tumors in the Army series studied by Blades[1] and in the personal experience of Brewer and Dolley.[6] The high incidence of thymic tumors in the present study undoubtedly reflects the interest of this clinic in the relation of the thymus and thymectomy to myasthenia gravis.[2, 3] If the eight patients with thymoma associated with myasthenia were to be omitted, the resulting frequency of thymoma in the survey would be identical with that of teratoma. The small number of dermoid cysts noted in this study is worthy of comment, as Heuer and Andrus considered dermoids and teratomas as a group to be the commonest tumors of the mediastinum.[16] Figure 16 shows the percentage distribution in the present series of the commoner types of tumor and their usual position in the mediastinum.

The diagnosis of mediastinal tumors has been ably discussed recently by Brewer and Dolley.[6] As stressed by these authors, the important considerations in differential diagnosis are malignant and benign tumors of the lung, aneurysms, tuberculosis of the mediastinal nodes, and diaphragmatic hernia. The present survey emphasizes the difficulty of accurate, specific, preoperative diagnosis of primary mediastinal tumors. In 101 patients, without separation into the finer histologic categories, 26 distinct varieties of tumor were identified. Fourteen of the tumors were "survey lesions." Other than the association of the manifestations of myasthenia gravis with thymoma, of hyperparathyroidism with mediastinal parathyroid adenoma, and of compression of the cord with a few of the neurogenic tumors of the dumb-bell type, no symptoms or signs were observed in this group of patients which could be related to a specific type of mediastinal tumor.

Clinical manifestations frequently offer little help in the pre-operative differentiation of benign and malignant tumors of the mediastinum. As pointed out by Heuer and Andrus,[16] Brewer and Dolley,[6] and others, the malignant tumors are more apt to be associated with evidence of rapid growth, pleural effusion, marked constitutional symptoms, obstruction of the superior vena cava, and paralyses of nerves. In the benign and malignant tumors of the present study, however, manifestations of this type were present in only a small percentage of either group. In Table II the incidence of various symptoms which accompanied benign and malignant tumors is set forth. As seen in the table the differences between the two groups, with few exceptions, are relatively insignificant.

Even though radiologic examination of the chest is undoubtedly the single most valuable diagnostic aid in the preoperative recognition of mediastinal tumors, a specific diagnosis can rarely be made with certainty. Fluoroscopy and the various specialized technics of angiography, kymography and laminography are of importance in excluding aneurysms and intrapulmonary lesions. The radiologic definition of the contour and position of the tumor in the mediastinum has the greatest practical significance for the surgeon. The frequency with which the tumors in the present study were in the various divisions of the mediastinum is shown in Table III.

The multiplicity of histologic types encountered in this survey and the limitations of diagnostic methods indicate that extensive delay in an effort to establish a specific diagnosis of mediastinal tumor prior to surgical exploration is unwarranted. Exploratory thoracotomy with biopsy or excision of the tumor has proved to be the most satisfactory means of establishing diagnosis and effecting treatment. The surgical approach is largely dependent on the position of the tumor. In the present series, because of the preponderance of anterior mediastinal lesions, anterolateral thoracotomy has been used most commonly. Tumors in the superior mediastinum have frequently been approached by median sternotomy; posterolateral thoracotomy has usually been employed for neurogenic tumors and other posterior lesions. An anterior transverse incision with division of the sternum and extensive exposure of both pleural cavities has been useful in the excision of large anterior tumors. In the 90 patients who were submitted to operation there were 55 benign lesions, 48 of which were successfully excised. Radical extirpation of the tumor was possible in only 9 of 35 malignant neoplasms. Follow-up studies on the entire group of patients are presented in the appendix.

SUMMARY

In order to obtain an estimate of the frequency and distribution of mediastinal tumors a survey has been made of 101 patients with primary neoplasms and cysts of the mediastinum observed during the last 18 years at the Johns Hopkins Hospital. There were 60 benign and 41 malignant lesions. Tumors of neural origin were most frequently encountered, followed by thymomas and the various types of cysts. Twenty-six different histologic types of primary mediastinal tumor were identified. Characteristics of the various tumors are discussed and illustrated. Pertinent data concerning individual cases and follow-up studies are summarized in an appendix.

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