

MALIGNANT THYMOMA*

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IN his inaugural dissertation to the University of Heidelberg in 1900, Grandhomme¹ applied the term thymoma to all malignant tumours of the thymus regardless of their histological structure. It soon became apparent that Grandhomme had proposed in effect to group together a number of different conditions of neoplasia, using the simple criterion of their topography to indicate relationship. This position was untenable for a number of reporters, among whom was Symmers² who objected to the use of the term thymoma, since it conveyed no impression of a particular morphological picture, while on the contrary a number of authors reserved it for carcinoma and others insisted it be used to designate sarcoma. Symmers implied that it could logically be applied only when the precise structural elements of the thymus were reproduced by the tumour. Decker³ pointed out that this attitude was, to say the least, inconvenient, since in no reported instance has a complete structural reproduction occurred, and suggested that the term be retained in its introductory sense or be dropped entirely and replaced with Ewing's classification.⁴

Ewing's classification is unacceptable because of his belief that all malignant thymomas are derived from the epithelial cells of the thymus. The belief that all intrinsic cells of the thymus are derived from the epithelial reticular cells of the organ is in direct opposition to the opinion of the vast majority of pathologists and histologists who accept the presence of both epithelial and lymphoid cell systems. The opposing school of thought has largely maintained its position on Ewing's negation and refuses to accept the independence of a lymphoid series until someone proves the small round cells, about which the debate persists, to be dissimilar from the epithelial cells. All efforts in this direction have but added evidence to the case for an independent lymphoid series. These efforts are perhaps best summarized by Cowdry:⁵

"Small cells of the thymus not only look like lymphocytes but are lymphocytes. The most detailed comparison of nucleus and cytoplasm with contained mitochondria fails to afford a single morphological distinction between 'thymocytes' and ordinary small lymphocytes of lymph nodes and blood stream. Both behave in the same way. They exhibit the same type of amoeboid movement and are capable of transformation into plasma cells. They are equally susceptible to roentgen radiation, and are agglutinated and cytolized by the same specific serum."

Aside from further arguments set forth by Dantchakoff,⁶ Pappenheimer,⁷ Hammer,⁸ and Maximov,⁹ the evidence submitted by the pathologists who sought the characteristics of a combined lymphoid and epithelial organ in conditions of disease has been overwhelmingly in line with this viewpoint. True lymphoid follicles have been demonstrated in the thymus in hyperthyroidism by Barton and Branch¹⁰ and in cases of myasthenia gravis, Addison's disease and acromegaly by Sloan.¹¹ Indeed, the wide variation in the size of the gland, reflected in conditions of involution both of age and accidental nature as well as hyperplasia, is mainly concerned with alterations in lymphoid content.⁸

For these and numerous other reasons the existence of an independent lymphoid system has seemed to us an unavoidable conclusion.

The lymphoid system in the thymus becomes established by migration of lymphocytes into the primitive epithelium of the organ early in the fetal life. The lymphocytes ultimately form dense round-cell masses in the cortex and most importantly diffusely infiltrate the medulla. It is pertinent to note here that the lymphocytes become established by migration into the organ. This process of establishment is rather unique in the sense that there is no hint of origin *in situ* from a pre-existing reticulo-endothelial system. Although tissue histiocytes exist there is no evidence to support their participation in **lymphoid histogenesis**.

In the medulla the epithelial elements appear in a ramified reticular form. Secondarily, the central epithelial cells hypertrophy and form the well-known Hassall's corpuscles. These epithelial reticular cells vary in their morphology and, in certain variants, can be seen to approach closely the appearance of lymphocytes which have an eccentricity in their own right. There is thereby created a zone of cell variation where the lymphocytes simulate reticular cells and conversely epithelial cells simulate lymphocytes. The schematic representation of these two cell systems seen in Fig. 1, illustrates the genuine closeness of this relationship in morphology.

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At this point the possibility of the confusion of two types of tumour arising through the existence of two closely similar although different small cells becomes worthy of consideration. Our series of cases which for a long time defeated diagnosis on a histological basis became clear when viewed with this in mind. The lymphosarcoma group are limited by the variations reached by the small and large lymphocyte. On the other hand, the epithelial reticular cell tumours extend from small polygonal cells of dimensions approaching that of a lymphocyte on the one extreme, to enormous multilobed or multinucleated giant cells on the other. Between these lie large cells whose epithelial identity is accepted. With this scheme in mind the conflicts, and the almost unalterable confusion in the literature, are easily understood.

An attempt was made by Crosby,¹² in 1932, to bring together the cases appearing in the literature since Rubaschow's¹³ collection of 69 cases in 1900, by shunting cases diagnosed as lymphosarcoma, lymphadenoma, thymoma, sarcomatous thymoma, lymphocytoma, etc., into the sarcoma group and cases labelled under some variation of thymic carcinoma into the carcinoma group. As a consequence, epithelial reticular cell tumours as well as lymphosarcomas are represented in both groups and contribute to both groups a set of clinical and pathological characteristics that are supposed to be distinctive for each group. Subsequent reports have accepted these statistical summaries and have incorporated them with concepts of the specific nature of thymic sarcoma on the one hand and carcinoma on the other.

A histogenic analysis of the cases classified as sarcoma reveals cellular tumours which range from small round cells belonging properly to the lymphosarcomas to multilobed and multinucleated giant cells of the epithelial series. The results of pursuing such a course are obvious.

To this point in our paper, we have, in a general way, endeavoured to clarify the problem of the malignant thymomata by indicating their histogenic nature. A discussion of the position of the two cell types in thymic oncology and an analysis of these specific cell types in representative cases follows.

MATERIALS AND METHODS

There were available in the files of the Department of Pathology of The Montreal General Hospital, eleven necropsied cases of malignant

thymoma in a total of 7,500 autopsies over a period of 25 years; an incidence of 0.014%. Symmers² reported an identical incidence. For study, our cases were subjected to routine hæmatoxylin-eosin stains and as many as possible to Masson's trichrome, Giemsa's polychrome, Laidlaw's reticulum stain and phosphotungstic acid hæmatoxylin.

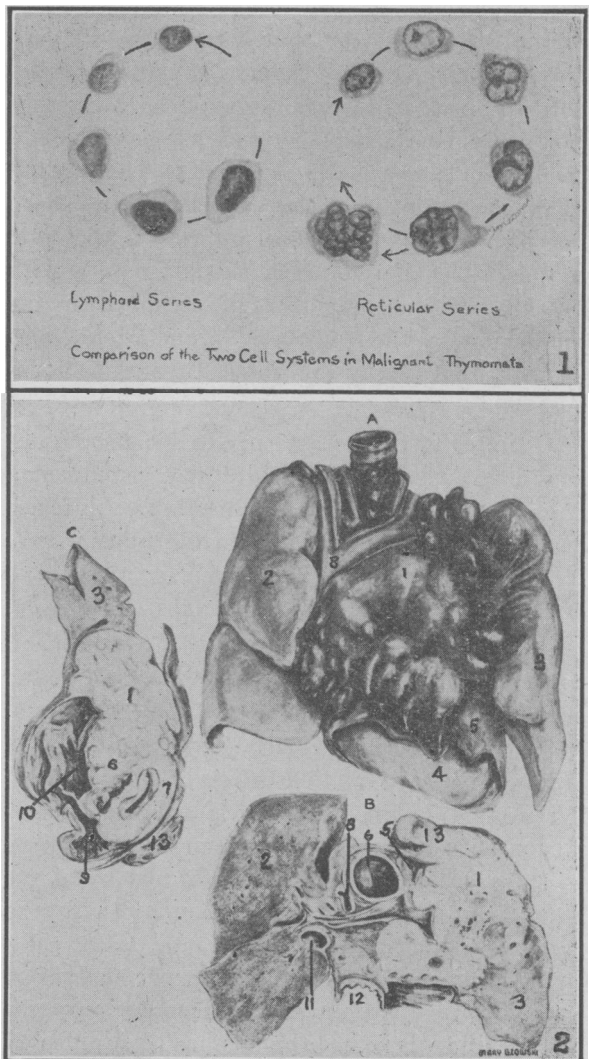


Fig. 1.—This diagram demonstrates the close morphological relation between the cells of the lymphoid series and cells of the reticular series. Note the tendency toward larger size, cytoplasmic and nuclear pleomorphism, and irregular chromatin dispersion in the reticular series. Fig. 2. (Case 4).—Malignant thymoma of lymphoblastic sarcoma variety. (A) Illustrates the tumour *in situ*. (B) Is a cross section taken at the commencement of the superior vena cava. (C) Is a cross section drawn at the level of the auricular introitus.

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| 1. Tumour. | 8. Superior vena cava. |
| 2. Right lung. | 9. Right auricle. |
| 3. Left lung. | 10. Left auricle. |
| 4. Heart. | 11. Right bronchus. |
| 5. Pericardium. | 12. Oesophagus. |
| 6. Aorta. | 13. Thymus. |
| 7. Pulmonary artery. | |

Our eleven cases were selected on the basis of the following criteria: (1) anatomical position; (2) method and degree of extension; (3) gross characteristics; and (4) histological analysis.

Regarding the anatomical position it is obvious that the main tumour mass occupies and extends from the locale of the thymus in the anterior and superior mediastinum. The cervical extensions of the normal thymus merit special attention, for these may easily explain the proclivity of many thymic tumours to extend into the neck. Moreover, they form a close, if not direct connection, between the cervical and mediastinal lymphatic systems. The lymph channels drain into the superficial and deep cervical lymph nodes and anterior mediastinal glands. The efferents from the latter unite with tracheo-bronchial glands and account for the similarity to the course of bronchogenic carcinoma that many of these thymic tumours pursue.

Ordinarily, in the case of thymic neoplasms, one may expect to find continuity of extension into the neck, middle mediastinum, inferior mediastinum, or laterally into the lungs.

In the selection of our cases we have been especially hesitant about accepting tumours which involve the mucosal surface of the bronchi, and present themselves with their main tissue mass in the middle and posterior mediastinum. The danger here, especially acute when one is dealing with an anaplastic and highly undifferentiated carcinoma, is the possibility of confusion with bronchogenic tumours. The spread of these to the tracheomediastinal nodes and the subsequent lymphatic permeation much in the same course as that of thymomata has already been emphasized. Pathologically, the absence of bronchial involvement and pulmonary suppuration in tumours of the thymus has been reflected clinically in the infrequency of a productive cough.

Concerning the gross characteristics a great deal of variation in consistency and colour is seen, depending upon the integrity of vascular supply and the degree of attendant fibrosis. For the most part the tumours are creamy white in colour, firm in consistency, and smooth in texture. This does not aid much in identification but the lobulation of the exterior is more unique (Fig. 2). Necrotic areas are usually present but these generally do not attain the dimensions of massive softening.

For an orderly appreciation of the histological characteristics of these tumours some sort of systematization is necessary. The term thymoma we believe should be applied to conditions of neoplasia arising from either the lymphoid or epithelial system of the thymus. We therefore propose to discuss the groups of thymic neoplasms which have their histogenesis in either component. For convenience these can be classified as follows:

MALIGNANT THYMOMA

- A. Thymic carcinoma.
 - 1. Diffuse reticular.
 - (a) Small cell.
 - (b) Large cell.
 - (c) Giant cell.
 - 2. Simple.
 - (a) Medullary.
 - (b) Alveolar.
 - (c) Adeno.
 - (d) Epidermoid.
- B. Thymic sarcoma.
 - 1. Lymphocytic.
 - 2. Lymphoblastic.
- C. Associated with systemic entities.
 - 1. Leukæmia.
 - 2. Hodgkin's.

As a matter of convenience for demonstrating the relations between cells of these different tumours the sarcomata are presented first.

THYMIC SARCOMA

This major group is readily divisible into lymphocytic sarcoma and lymphoblastic sarcoma. Other tumours may arise from mesenchymal elements but the importance of these derivatives is negligible from the standpoint of specific thymic structure or function. Hence they are not considered as thymomata from other than a topographical grouping.

The relation between lymphocytic and lymphoblastic sarcoma is well-known and needs no further elucidation.

LYMPHOCYTIC THYMOMA

These tumours consist of small round cells with compact nuclei and defy differentiation from lymphocytic sarcoma elsewhere. Their uniformity would seem to exclude the possibility of confusion with thymic carcinoma but such an exclusion is more apparent than real. Case 5, of the following reported cases, a predominantly small cell reticular carcinoma, demonstrates this fact well. Scattered among cells which are to all apparent purposes lymphocytes are cells of giant dimensions, whose derivation is obviously not lymphoid, which are in every way identical with the cells seen in pure and

unmistakably reticular tumours, and whose relation to the small cells can be traced through transitional forms. For the purposes of comparison the following three cases of lymphocytic sarcoma should be kept in mind.

CASE 1

Clinical examination.—Male, C.B., aged 23, was well until February, 1937, when he began to feel continually tired. In March he developed a dry, unproductive, hacking cough. In April he was admitted to a New York hospital when a diagnosis of thymoma was made. After ten days' treatment with x-ray he felt greatly improved and was discharged.

In May, 1937, his symptoms returned and he was admitted to this hospital with the additional complaints of dull crampy pains in the left chest and a sense of obstruction in his throat.

Physical examination revealed a space occupying lesion of the left chest with loss of distinction of the cardiac area. Temperature 98°, pulse 92, blood pressure 120/80, respirations 22.

Laboratory examinations.—*Roentgen:* Shadow extending above the aortic arch to the left side and small amount of fluid in the left base. *Pathological:* Pleural fluid: heavy deposit of lymphocytes, without mitotic figures, but whose clumping suggests malignancy. *Hæmatological:* Red blood cells 4,400,100; white blood cells 7,400; polymorphonuclears - 70%; lymphocytes 20%; monocytes 10%; Hgb. 10.5 gm. *Metabolic:* Basal metabolic rate, plus 15.

Clinical course.—Aspiration of the left chest was commenced immediately and x-ray therapy was instituted on June 3, 1937. He was given 1,700 to 2,000 R.U. to June 25, and symptomatic improvement followed. July 28 marked the beginning of abdominal and testicular symptomatology as well as an increase in the severity of his respiratory distress. Despite another course of x-ray therapy he became weaker and died on October 24, 1937, with signs of generalized sarcomatosis.

PATHOLOGICAL SUMMARY

Gross findings.—On opening into the thoracic cavity, a tumour was found lying in front of the heart. It was irregular and pear-shaped, measured roughly 3 cm. in length, and consisted of two lateral lobes and a central isthmus. From the central isthmus there extended anteriorly a tumour mass which was whitish, rubbery, and mobile.

The pleural layers of both cavities were grossly invaded by marble white tumour. The only invasion of the lung was in the form of a 1.5 cm. round firm nodule in the hilus of the left lung. The right lung was collapsed.

The tumour had grown down the posterior mediastinum, chiefly on the left side, and enclosed the descending aorta and œsophagus, developing a traction diverticulum of the latter. After involving the superior aspect of the diaphragm it descended between the crura posteriorly into the retroperitoneal space where it extended in a series of continuous nodules to the level of the 3rd lumbar

vertebra. At the region of the spleen and kidney it came forward on the left side while on the right it was in close association with the kidney pelvis.

Microscopical findings (Fig. 3).—Sections of the tumour and metastatic sites show a cellular mass composed of remarkably uniform small round, oval, and polygonal shaped cells supported by a delicate vascular connective tissue stroma which merges into denser strands dividing the tumour into small lobules and sheets. These discrete and uniform cells are of the dimensions of adult lymphocytes with dark nuclei and scanty cytoplasm. There is a notable lack of pleomorphism and absence of cells of epithelial or giant dimensions.

Diagnosis.—Malignant thymoma of the lymphocytic sarcoma variety. Extension to left pleura, hilus of left lung, retroperitoneal space, pancreas and periadrenal tissue. Metastasis to mediastinal, upper abdominal, right and left axillary nodes, kidneys, right tunica vaginalis, and testis and cord.

CASE 2

Case submitted for autopsy from outlying hospital. No clinical history available.

PATHOLOGICAL SUMMARY

Gross findings.—Upon opening the thorax, the mediastinum was seen to be invaded by a large solid mass bounded on both sides by the lungs. Posterior to the mass lay the œsophagus, trachea, and descending aorta all of which were somewhat compressed by the tumour.

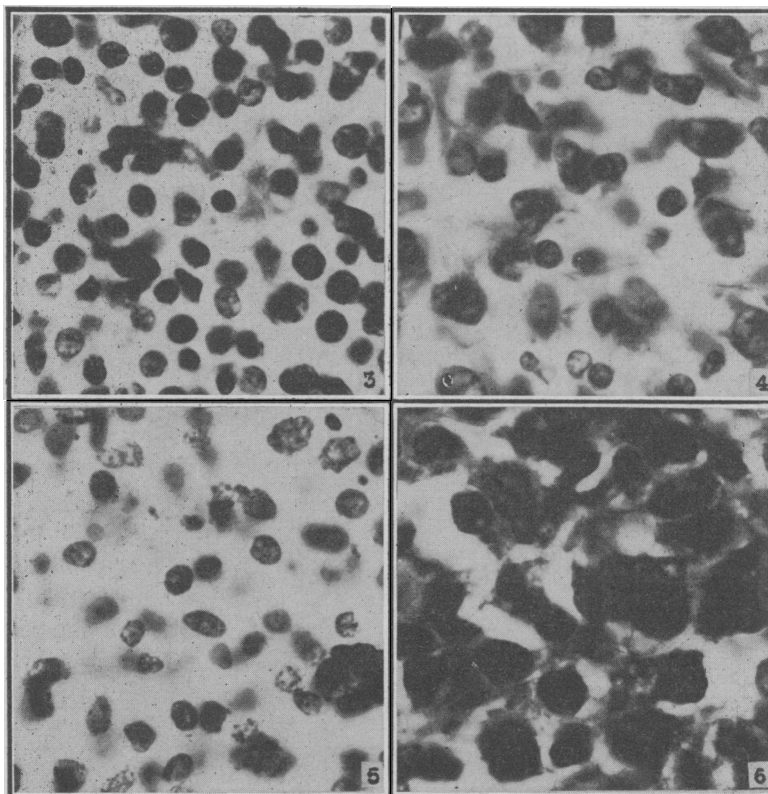


Fig. 3. (Case 1).—Lymphocytic sarcoma. Note the regularity in cell and nuclear size and relatively even dispersion of nuclear chromatin. **Fig. 4.** (Case 4).—Lymphoblastic sarcoma. Note the transitions between cells of the larger and smaller orders but absolute absence of giant cells. The smaller cells are identical with adult lymphocytes, the larger with immature lymphoblasts. **Fig. 5.** (Case 5).—Diffuse reticular cell thymoma of the small cell variety. Note the predominance of small cells with variation extending to the giant multilobed cells. **Fig. 6.** (Case 6).—Malignant thymoma of the large cell reticular variety. Note the relatively large, irregular, pleomorphic cells with the transition to large multilobed giant cells.

The two main bronchi passed through it. They were not invaded grossly but were somewhat narrowed by compression. On the superior aspect, the arch of the aorta and ascending branches also passed through the tumour mass without being invaded. On the right border lay the superior vena cava which was almost completely flattened but not invaded. The left innominate vein met the right at the superior lateral aspect and was plugged with a thrombotic mass. The whole of the anterior mediastinum was a solid mass of tumour which had grown down over the pericardium where at its base it measured 3 cm. in thickness. Over the left ventricle the pericardium had been invaded and the heart itself covered by a rough nodular jacket of tumour. Where the lungs were adherent to the tumour mass the pleura and lung for a distance of 4 cm. were invaded at the hilus.

Microscopical findings.—The tumour mass is composed of closely packed small round cells with compact densely staining nuclei and scanty cytoplasm. There is no other cell type in evidence. Mitotic figures are infrequent. A section through the lung hilus consists of large cartilaginous bronchus surrounded by tumour which extends into the bronchus between cartilages, about the mucous glands in the submucosa but does not involve the mucosa itself except at one small area, where it extends right up to the thickened basement membrane. About the bronchus tumour can be seen in some of the veins, both in the lumens and infiltrating the walls. Sections of the involved lymph nodes show almost complete replacement with tumour which is seen to be travelling in the afferent channels. Sections of adrenals show invasion only at their margin from the peri-adrenal fat.

Diagnosis.—Malignant thymoma of the lymphocytic sarcomatous variety. Extension to pericardium, heart, bronchi, and veins of lungs. Metastases to para-aortic abdominal nodes, and peri-adrenal and adrenal tissues.

CASE 3

Clinical examination.—Male, A.S., aged 18, was well until March 21, 1925, when two weeks previous to admission, he noticed difficulty in breathing and excessive fatigue. A non-productive cough and difficulty in swallowing developed in the following week.

Physical examination revealed a space-occupying lesion of the right chest extending upward into the neck anteriorly. Compression of superior vena cava by a mediastinal neoplasm with congestion of facial veins was evident. Temperature 98.6°, pulse 102, blood pressure 120/90 and respirations 28.

Laboratory examination.—*Roentgen:* Anterior mediastinal growth with right-sided pleural effusion and displacement of the heart to the left. *Pathological:* Small lymphocytes and eosinophiles in aspirated fluid from pleura. *Hematological:* Red blood cells 5,350,000; white blood cells 18,200; polymorphonuclears 62%; lymphocytes 20%; eosinophiles 16%; monocytes 2%.

Clinical course.—Frequent chest aspirations were carried out but patient declined rapidly and died on June 17, 1925, after progressive dyspnoea, cyanosis, and chest pain.

PATHOLOGICAL SUMMARY

Gross findings.—The intrathoracic tumour consisted of a large mass situated above and to the right of the pericardium from which it could not be separated, and was continuous with the anterior cervical lymph nodes. The outer margin pressed upon and constricted the superior vena cava and was adherent to the medial surface of the right lung. Greyish white nodules extended over the parietal and visceral pleura of this lung, which was collapsed and surrounded by 3.5 litres of fluid. From the hilus the tumour could be followed toward the base of the heart where the right pulmonary artery was compressed by the tumour but the pulmonary veins not involved.

While the left lung demonstrated no gross lesion, the right was invaded at the hilus by a neoplasm which

extended out into the parenchyma as tongue-like processes becoming nodular terminally.

Microscopic findings.—The main tumour and its metastatic sites is composed of a diffuse and uniform cell mass. These cells are discrete, small, generally round and contain scanty eosinophilic cytoplasm. The nuclei are quite round and compact with no uneven dispersion of chromatin. Hyperchromatic pleomorphic cells are notably absent.

Diagnosis.—Malignant thymoma of the lymphocytic sarcoma variety with invasion of the right lung, pleura, lymph nodes of the cervical chain, and superior surface of the right dome of the diaphragm.

LYMPHOBLASTIC SARCOMA

The larger cell size, as well as the greater pleomorphism which characterizes these tumours, increases the likelihood of their confusion with the reticular cell group. They fall into the cell size range occupied by the more frequent large cell reticular thymomata. Fortunately several characteristics are sufficiently dissimilar to make differentiation possible.

1. The variation in the cell size which the large cell reticular carcinoma produces tends toward the giant order while the variations in cell size which the lymphoblastic sarcoma demonstrates tends toward the lymphocytic side.

2. In the reticular cell tumours the cytoplasm tends toward greater basophilia, irregularity in contour, and intensity.

3. The variation seen in the nuclear shape of the lymphoblastic group is typified by oval, elongated, and indented forms. The nuclear variation of the reticular cell thymoma is apparently without limitation and assumes the most bizarre shapes and forms.

4. The chromatin content of the nucleus in the lymphoblastic sarcoma is generally evenly dispersed while in the larger reticular cells it is unevenly distributed with large irregular deposits standing out in a pale nucleoplasm.

5. Mitotic figures and anaplasia are generally more evident in the reticular group.

For purposes of comparison the following case of lymphoblastic sarcoma should be studied in relation to cases six and seven of the reticular cell group.

CASE 4

Clinical examination.—Female, F.C., aged 19, was in excellent health until January, 1944, when she developed pain in the left shoulder. At the same time she noted the onset of an unproductive cough. In June she developed pain in the left upper chest. One month previous to admission she suffered from a severe attack of laryngitis and at the time of admission was hoarse. For the week preceding admission the cough was productive of a slight amount of whitish sputum. During the last two months there had been a weight loss of fifteen pounds associated with a loss of energy. No other complaints referable to any system could be elicited on inquiry.

Physical examination revealed evidence of a space occupying lesion of left chest and substernal area with tracheal displacement to the right. Blood pressure 105/74, pulse 90, and respirations 20 per minute.

Laboratory examination.—*Roentgen*: General appearance of anterior mediastinal tumour rather than a lesion of the lung itself. *Hæmatological*: Red blood cells were reduced to 3,950,000; white blood cells 7,600. Lymphocytes constituted 43% of the cells. *Pathological*: Biopsy diagnosis of tissue from anterior mediastinal tumour at operation was malignant thymoma.

Clinical course.—A tentative diagnosis of anterior mediastinal tumour was made with secondary paralysis of the left phrenic and left recurrent laryngeal nerve. An exploratory mediastinotomy was undertaken by Dr. Fraser B. Gurd, on August 8, 1944, who felt that the tumour might be benign in character. It became apparent upon opening into the anterior mediastinum that removal of the tumour was impossible. It was Dr. Gurd's intention to press the employment of x-ray radiation should the patient survive the surgical interference, but death occurred on the day following operation.

PATHOLOGICAL SUMMARY

Gross findings (see Fig. 2).—On opening into the thoracic cavity the left lung was found collapsed and there was a pneumothorax of the left pleural cavity.

The mediastinal mass was bounded anteriorly by the sternum and anterior thoracic wall, posteriorly by the œsophagus, laterally by the pleura of the left lung, and medially by the right lung. Superiorly it was limited by the left innominate vein while inferiorly it extended to within 2 cm. of the lower heart margin. It measured 12 by 10 by 8 cm. The presenting surface was convex and nodular and its lower margin extended downward in irregular finger-like projections. In colour it was light pink while the consistency was firm.

The main mass lay to the left and extended into the upper lobe of the left lung which had been pulled medially by constricting outgrowths of tumour. The superior vena cava ran beneath the right superolateral margin of the tumour which compressed the vessel. Posteriorly and superiorly it surrounded both the aorta and pulmonary artery, constricting them, and continued around the left main branch of the latter to lie in close approximation to the œsophagus. It had insinuated itself behind the left innominate and great arteries to the head and neck to lie against the trachea above. It was in this region that the left recurrent laryngeal and left vagus nerve were buried in the tumour. In front it rested against the parietal pericardium, following it to the lower margin of the heart and attached itself to the surface of the heart there.

The right lung showed no evidence of tumour. In the left lung, the lower lobe was free of tumour but the upper lobe was extensively invaded by outgrowths becoming confluent and solid in the parenchyma. It extended to the inter-lobe septum and to the pleural margin laterally, but did not project from the mucosal surface of any of the bronchi although involvement of their walls and compression of the lumina were obvious.

The other organs with the exception of the adrenals showed no gross lesion. Both adrenal cortices were thickened and the medullary areas replaced by firm, light yellow tissue.

Microscopical findings (see Fig. 4).—The main tumour mass and its metastatic sites demonstrate a diffuse cell picture composed of cells varying from the dimensional order of small lymphocytes to cells two and a half times as large (6 to 15 μ). These are intimately related to an evenly distributed and heavy reticulum consisting of fine and coarse fibrils. A collagenous stroma in the form of coarse trabeculae divides the tumour into irregular lobules while a few delicate collagenous fibres intertwine between lobules.

The majority of the cells are of the large order and when compared with the smaller are seen to contain more abundant and irregular eosinophilic cytoplasm,

larger and more pleomorphic nuclei. These are preponderantly oval in form, have a granular dispersed chromatin, eosinophilic nucleoli, and moderate numbers of mitotic figures. The small cells on the other hand are definitely rounded with scanty cytoplasm. The nuclei are generally round and compact with little or no dispersion of chromatin, no visible nucleoli, and no apparent mitotic figures.

Diagnosis.—Malignant thymoma of the lymphoblastic sarcoma variety. Extension into the neck, hilus of the left lung, pericardium, myocardium, superior vena cava, left vagus and recurrent laryngeal nerves, cardiac nerves, left bronchus, and peribronchial nodes. Metastases to both adrenals and ovaries.

CARCINOMA

Regarding this major category we have only a few additional points to discuss. It should be borne in mind that the reticular cell tumour is the most difficult of all malignant thymic neoplasms to define. It presents a most varied picture. Predominantly small cell, large cell and giant cell tumours can be distinguished but in all the cases collected more than one cell type has been found. In considering all these epithelial cell tumours one should especially be aware of the lymphocytes which frequently infiltrate the tissue rather heavily and obscure the picture. Or conversely, the tumour may heavily infiltrate preformed lymphoid tissue. This is but to be expected in an organ which is composed of both elements. The presence of lymphoid tissue and the inability to differentiate malignancy from infiltration has led authors to call these tumours lymphoepithelioma, lymphocarcinoma, etc. Ewing,⁴ Matras and Priesel²³ and others have drawn attention to the passive nature of the lymphocytes.

The medullary and alveolar subdivisions of the carcinoma group differ markedly from the diffuse reticular tumours, although their relationship has been demonstrated by MacDonald,¹⁴ in his series of apparently transitional cases. These tumours consist of solid sheets, cords or alveolar groupings of epithelial cells and are easily differentiated from the sarcomata. Because of their dissimilarity from diffuse reticular cell tumours, their occurrence in a distinct age group, and the finding of almost pure adenocarcinoma among them, the possibility of an origin from a persistent thymic duct should be worthy of consideration.

However, all that can be demonstrated at the moment is that the thymic epithelial cell has the potentialities for development in at least three directions. One is toward the reticular cell, another toward Hassall's corpuscles, and a third reverts to the more familiar primitive cell which

may in turn differentiate into medullary, alveolar, adeno, and even epidermoid forms of carcinoma. The representation of variations of these combinations present in the literature is an extremely interesting feature of thymomata.

Diffuse reticular cell thymoma.—The main characteristics of diffuse reticular cell thymoma have already been outlined in summarizing the details of dissimilarity from the sarcomata and need no more elucidation here. Of the cases that follow, Case 8, is particularly interesting from the standpoint of demonstrating the relationship which exists between the diffuse reticular cell tumour and the more common varieties of ordinary carcinoma. The primary site reflects the pleomorphic, mixed reticular cell picture and two metastatic sites show different conformations again. One is almost purely medullary carcinoma, the other adenocarcinoma.

CASE 5

Clinical examination.—Male, W.M., aged 56, was admitted January 3, 1932, with complaints of pain in the epigastrium and dyspnoea. His history dates back to July, 1931, when he noted swelling of the ankles. Four months later his voice became soft and weak. In the latter part of December, he suffered from an attack simulating angina. Three days before admission his precordial pain became severe and persistent.

Physical examination revealed râles at the bases of both lungs and tenderness over the abdomen. No signs of his primary condition were present.

Laboratory examination.—Without significance.

Clinical course.—Decline was rapid and he died on January 6, 1932, three days following admission.

PATHOLOGICAL SUMMARY

Gross findings.—Upon opening the peritoneal cavity a suppurative peritonitis and perforated duodenal ulcer was found.

In the thoracic cavity a large mediastinal tumour was found which extended anteriorly to the sternum, superiorly to the clavicles, inferiorly to the lower margin of the left auricle, and laterally to the hila of both lungs. Encircling the ascending aorta, it could be followed under the arch where, posteriorly, it surrounded the trachea and main branches of the bronchi. The superior vena cava lay at the right margin of the tumour. The vessels, bronchi, and trachea were not invaded by the tumour. Although the hilar lymph nodes of both lungs were involved, no massive invasion of either lung had taken place. There was extension along the interlobar pleura of the left, however. The tumour was greyish-white, lobulated and firm throughout.

Microscopical findings (Fig. 5).—This tumour resembles lymphosarcoma closely and consists of a compact cellular mass intersected by coarse connective tissue trabeculae. The cells, for the most part, are of the dimensional order of lymphocytes, but on the average a little larger. The cytoplasm is generally very pale, but well defined, and has rounded or polygonal contours.

The nuclei vary considerably from rounded to oval and elongated forms. Although containing considerable chromatin this is unevenly dispersed. Scattered throughout are cells of twice the dimensions and further transitions are seen in size until cells of forty micra are seen which are multinucleated and multilobed. Some of these giant cells are mononuclear and contain large oval nuclei.

All of these larger cells are extremely hyperchromatic and mitotic figures are fairly numerous.

Diagnosis.—Malignant thymoma of the diffuse small-cell reticular variety with invasion of the lungs.

CASE 6

Clinical examination.—Male, B.P., aged 32, was admitted June 29, 1944, complaining of pain in the back, legs, left shoulder and left arm. Both his right and left hands felt weak and his fingers numb. This history began in April with undue fatigue and loss of appetite. In the last six months he lost twenty pounds in weight and considerable strength. At the time of admission he was unable to even sit up.

Physical examination revealed apparent normality of the chest and abdomen. A tumour was seen filling the left temporal fossa. Palpable glands were present in each axilla. Weakness was noticed of both the left and right hands with thinning of the left hypothenar and thenar eminences. The patellar reflex could not be obtained and the abdominal reflexes were decreased.

Laboratory examination.—*Roentgen:* Marked soft tissue swelling on the left side of the head. In the chest there was an increase of the left hilar shadow with shadows extending out into the left lung field. The retropharyngeal space at the level of the fifth and sixth cervical vertebrae was widened. *Pathological:* Lymphosarcoma of the right axillary node. *Hæmatological:* Normal.

Clinical course.—In July fullness of the supraclavicular fossa was noticed and in August parasternal swelling and pain. The liver edge became palpable and on November 12, 1944, the patient died following the development of marked dyspnoea and anasarca.

PATHOLOGICAL SUMMARY

Gross findings.—On opening the body a large mass of tumour was seen lying immediately beneath the skin of the right thorax. This extended up from the substernal area through the suprasternal notch, had almost disarticulated the sternoclavicular joint on the right side, was attached to the pectoralis major on its deeper aspect, and involved the left subcutaneous tissues to the distance of 3.5 cm. on that side. It rose some 2 cm. above the clavicle and likewise infiltrated inferiorly reaching the ninth ribline where it blended imperceptibly with the muscular tissues on the right side. There was, then, a tumour occupying the right pectoral area, extending to the left of the mid-sternal line for a short distance, and continuous with a mass lying in the anterosuperior mediastinum.

In the thoracic cavity the tumour mass was attached to the parietal pericardium and was bound on both sides by the auricular appendages, and above by the origin of the great vessels to the head and neck. It measured roughly 4 by 6 cm. and was stony hard in consistency and white in colour. The cut surface had a lobulated appearance with small hæmorrhagic areas interspersed between lobules. Small nodules measuring about 0.3 cm. in diameter extended apparently without continuity down the lateral surface of the parietal pericardium, and on to the pleural surface of the right lung. The pericardium was distended with fluid as were the pleural cavities.

The surface of the right lung was peppered with tumour nodules. The larger portion of the base of the middle lobe was occupied by tumour which extended into, and occluded the middle lobe bronchus. The lower lobe bronchus was free although the tumour extended up to its margin at its origin. The upper two-thirds of the lower lobe of the left lung was occupied by tumour. This again was in intimate relation to the bronchus of that lobe and extended to the mucosa. There was no peribronchial adenopathy affecting nodes lying in close relationship to the tumour.

The abdominal cavity contained 3,000 c.c. of fluid. No larger masses of tumour were palpable in the cavity. However, small nodules could be palpated in the mesentery and in the greater omentum. Prevertebral tissue

was infiltrated with tumour for a depth of 1.0 cm. in the region of the fifth lumbar vertebra. This faded out so that none could be detected in the twelfth thoracic area. Likewise the precervical fascia was infiltrated as high as the thyroid cartilage and the brachial plexus was involved by the mass. This again, was continuous with the substernal tumour.

The rest of the gross examination was devoid of pertinent findings except for the left kidney whose subcapsular surface showed a small nodular metastasis.

Microscopical findings (Fig. 6).—The main tumour and its metastatic sites consist of a uniform cellular structure lying in intimate relation to a reticular network consisting of coarse and delicate fibrils. A collagenous stroma divides the tumour into lobules and in the lobules a finer stroma runs between cells.

The cells range in dimensions from 16 to 40 micra. The majority are of the smaller order with irregular polygonal outlines. Cytoplasm is abundant, opaque, and tends toward basophilia. Nuclei are bizarre and hyperchromatic. The multiplicity of nuclear shape is impossible to describe. The nuclear chromatin is gathered into unevenly dispersed deposits resulting in a vesicular appearance. Many contain large eosinophilic nucleoli.

Cells of the larger order are multinucleated and multilobed as well as mononucleated. Some of the multinucleated cells contain as many as eight nuclei while the multilobed cells show irregular foldings of the nucleus. These large cells are generally more hyperchromatic than the smaller cell and mitotic figures are numerous among them.

Diagnosis.—Malignant thymoma of the large cell reticular variety with massive extension into the supraclavicular area; metastases to the hilar region of the right lung, left lung and multiple metastases to the pericardium and pleura of the right lung, prevertebral and precervical tissues, and left kidney.

CASE 7

Clinical examination.—Male, P.H., aged 37, was admitted on January 5, 1922, complaining of swelling of his chest, cough, pain in the right chest and loss of fifteen pounds of weight.

The swelling had been noted eighteen months previous to admission. Inquiry revealed that he had had a cough with expectoration in the morning for several years and night sweats for about five months.

Physical examination revealed a very large, irregular tumour occupying the front of the chest and enlarged left anterior cervical and axillary glands. These were firm and discrete.

Examination of the chest was negative except for the area occupied by the tumour. Although there was no apparent displacement of the heart, the right border was marked 7 cm. beyond the sternal margin and a diffuse pulsation of the tumour appeared to be transmitted from the heart. Heart sounds at the apex and base were distant but otherwise normal.

Laboratory examination.—*Roentgen*: Showed a large, dense, homogeneous soft-tissue shadow anterior to the bony thorax, definite enlargement of the right hilar shadow, and increase of the heart shadow to the right. *Pathological*: Pleural fluid showed a predominance of large and small lymphocytes and malignant cells with mitotic figures. Undifferentiated type. *Serological*: Blood Wassermann, four plus. *Hæmatological*: No reduction in red blood cells. White blood count 8,500, of which 7% were eosinophiles. Otherwise normal hemogram.

Clinical course.—In February, the patient began to run intermittent fever with peaks of 102.4° which persisted until his death. The essential symptomatology remained unchanged except for the appearance of an enlarged liver on June 12 dullness over the flanks, and a pericardial friction rub. The superficial tumour resolved partially after several courses of x-ray therapy but increased in its intrathoracic part. In June signs of rapid decline commenced with increasing cough and expectoration, loss of weight and profuse sweating. He expired on July 3, 1922.¹

PATHOLOGICAL SUMMARY

Gross findings.—Occupying the central portion of the subcutaneous tissue of the thorax and commencing one inch below the upper border of the manubrium and extending downward to the xiphoid cartilage and laterally to the nipple line on either side was a large nodular mass measuring approximately 17 by 15 by 5 cm. The surface of this mass was irregular and the skin over it was fixed to the underlying tissues. On cutting through the skin the tumour was seen to be nodular and extended through the sternum to become continuous with a retrosternal mass.

The greater part of the anterior mediastinum was replaced by tumour which invaded the pericardium, pleura, right lung, diaphragm, and mediastinal glands. The tumour was pale and greyish white in colour, homogeneous in nature and fairly firm in consistency.

The tumour had invaded the parietal and visceral layers of the pericardium on the supero-lateral aspect and had penetrated the epicardium on the right side. The right lung had been invaded by tumour predominantly in its middle and lower lobes. About the visceral pleura were scattered numerous nodular metastases. There was a caseous tuberculous nodule of the apex of the left lung.

In the peritoneal cavity the lower surface of the diaphragm, liver, appendix, and retroperitoneal mesenteric glands were invaded by this growth.

Microscopical findings.—The cells constituting the tumour are closely packed. In size they average approximately twenty micra. Their cytoplasmic constituent is moderate but the nuclei are relatively large. Many of the latter contain nuclei which are themselves the size of small lymphocytes. The nuclear membrane is well defined and the chromatin is irregularly and sparsely dispersed resulting in a vesicular appearance. The majority consequently are hypochromatic although a few reach the opposite extreme. Mitotic figures are infrequent. Some nuclei show irregular foldings and bizarre shapes. Also scattered throughout are larger cells of giant dimensions some of which have very large irregular solitary nuclei while others are multinucleated and contain two to seven nuclei. There are no eosinophils and only a few passive lymphocytes. The metastatic sites show similar cellular characteristics.

Sections of the lungs show only a small amount of recognizable parenchymal tissue. The remainder consists of a solid cellular tumour mass in which there are incorporated blood vessels. Of these the pulmonary veins can be seen to be diffusely invaded by tumour. The general pattern of the tumour follows the general architecture of the lung.

Diagnosis.—Malignant thymoma of the large and giant cell reticular variety with extension to the right pleura, right lung, pericardium, diaphragm. Perforation of the sternum and spread in the subcutaneous tissues of the thorax. Metastases to the liver, appendix, and bronchial, supraclavicular, infraclavicular, axillary, retroperitoneal, and mesenteric nodes.

CASE 8

Clinical examination.—Male, F.P., aged 37, was admitted on February 8, 1939, complaining of a swelling extending into the neck from the chest, of three months' duration. This caused extreme dyspnoea, eventually hoarseness and a productive cough. There was fifteen pounds of weight loss in this three month period.

Physical examination revealed a substernal mass, cyanosis, dyspnoea and dilated superficial veins of the thorax.

Laboratory examination.—*Roentgen*: A lobulated mass involving the region of the aortic arch in front of the trachea. *Hæmatological*: Of no significance.

Clinical course.—Decline was rapid, with the development of a severe respiratory infection, progressive dyspnoea and emaciation.

PATHOLOGICAL SUMMARY

Gross findings.—Upon opening the thorax the entire superior mediastinum was seen to be occupied by a tumour mass measuring 12 by 7 by 9 cm. It was attached anteriorly to the manubrium and posteriorly to the trachea. It extended from 3.0 cm. above the supra-sternal notch down to the upper margin of the heart. Lobulation was the unique feature of its exterior surface and in conformation the tumour was roughly oval. The mass incorporated the superior vena cava, the first part of the aorta, and the great vessels to the head and neck. The veins were both compressed and infiltrated with tumour while the arteries were only slightly compressed. The consistency was firm and on cross section fibrous septa were seen to intersect the mass. Some softened areas of necrosis were interspersed.

Multiple sections of the lung and bronchi revealed no evidence of tumour.

Of the abdominal viscera only the mesenteric nodes and the adrenals showed any evidence of tumour. The left adrenal was enlarged and its interior was replaced by tumour tissue similar to that seen in the mediastinal site. The medulla of the left contains a few 2 mm. nodules of similar neoplasm.

Microscopical findings (see Fig. 7).—The main tumour site consists of a very pleomorphic cell mass. The cells are for the most part large and polygonal in shape although extreme variations in both contour and dimensions are present. A feature of this histological varia-

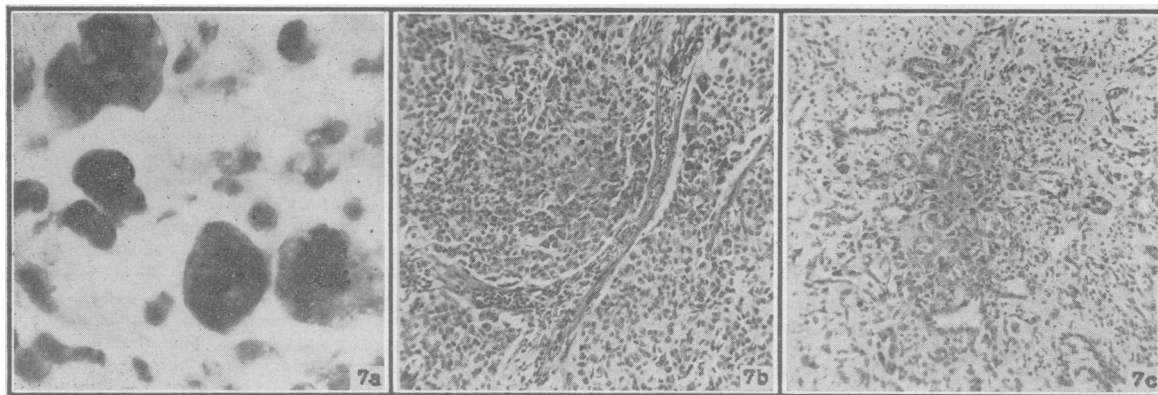


Fig. 7. (Case 8).—Diffuse giant cell reticular thymoma. (a) Shows giant cell constituents of primary tumour site. (b) Shows medullary conformation of metastatic tumour in left adrenal. (c) Shows glandular arrangement of metastatic tumour in right adrenal.

tion is the presence of many tumour cells of giant dimensions most of which are mononuclear. Some however are multinucleated and assume extremely bizarre forms containing bulky nuclei. Throughout there is as great variation in nuclear staining reaction as there is in cell shape but the general tendency is toward hyperchromatism.

Nowhere does the tumour invade the wall of the bronchi. Although the wall of the trachea is invaded, the growth does not involve the mucosal surface.

Sections of the left adrenal show replacement of practically the entire gland by tumour growth. Here the tumour cells are arranged in broad sheets of polygonal cells. Giant cells are present but are not nearly as numerous as in the parent tumour nor are they as large. In the right adrenal the tumour infiltrates the medulla widely and invades the cortex. An extremely interesting feature is the formation of gland-like spaces lined by tumour cells.

Diagnosis.—Malignant thymoma of the giant cell reticular variety and a transition to simplex and adeno type, with invasion of the trachea and superior vena cava and metastases to both adrenals.

SIMPLE CARCINOMA

This group has already been defined and its relation to the diffuse reticular cell tumours demonstrated both in the literature and in the preceding case. The case that follows therefore, needs no special comment.

CASE 9

Clinical examination.—Male, H.S., aged 47, entered the hospital November 4, 1927, complaining of pain in the chest, abdomen and swelling of the right side of the neck, of ten weeks' duration. The dyspnoea had become progressive and required him to adopt the orthopnoic position. Cough latterly became productive. Dilated veins on the thorax had been present for one month. The pain in the abdomen was burning in character.

Physical examination revealed a mass in the neck extending from below the right clavicle and marked substernal dullness occupying 7 cm. of the thorax on either side of the midline. Veins of the thorax were prominent and dilated. No abdominal findings reported. Temperature 98.6°, pulse 84, respirations 20 and blood pressure 160/90.

Laboratory examination.—*Roentgen:* A large shadow extending equally on both sides of the midline in the

superior mediastinum. *Hæmatological:* Red blood cells 4,500,000; white blood cells 10,200; polymorphonuclears 77%; lymphocytes 23%. *Serological:* Blood Wassermann plus three.

Clinical course.—Was progressive and rapid with increasing dyspnoea and signs of occlusion of the superior vena cava. Patient died on November 30, 1927.

PATHOLOGICAL SUMMARY

Gross findings.—A large firm tumour was present in the right side of the neck intimately associated with the great vessels of the right side. Its posterior boundary was the trapezius muscle and anteriorly it passed under the clavicle toward the midline to become continuous with a large mass occupying the greater portion of the superior mediastinum. Its lateral aspects in this position were covered by thin layers of the upper lobes of both lungs. Posteriorly the oesophagus and descending aorta were displaced to the left by the tumour. Posteriorly and laterally it invaded the hilar glands and although the lungs were intimately related to it they were not grossly invaded.

There were metastases to the axillary glands as well as the mesenteric nodes of the abdomen.

Microscopical findings.—The main tumour mass and its metastatic sites show a similar cytological structure. The cells are of moderate size, polygonal in shape, contain scanty ill defined cytoplasm and relatively large vesicular nuclei varying markedly in size and shape. They are generally hyperchromatic, vesicular and contain a large eosinophilic nucleolus. Mitotic figures are numerous.

The cells are arranged in broad sheets or anastomosing cords between which there is a delicate connective tissue stroma. In some places the cells are diffusely invading fat and connective tissue. Both veins and lymphatic vessels can be seen to be plugged with tumour. A perithelial arrangement of the cells is present in some areas but this arrangement seems to be due to survival of tumour about blood vessels in necrotic areas.

Diagnosis.—Malignant thymoma of the simple medullary carcinomatous variety with invasion of the lungs and superior vena cava and metastases to the cervical, peribronchial and periportal lymphnodes.

THYMOMA ASSOCIATED WITH SYSTEMIC ENTITIES

Having brought Hodgkin's disease and leukaemia into the folds of thymic oncology the problem of inter-relating these diseases more generally thought of as systemic entities becomes immediate. They affect the thymus in many instances and in some predominantly so. When the process can be proved to have arisen in the thymus, to have remained fairly well limited to its anatomical domain, and to conform to the criteria of other thymomata, their consideration must be that of a thymic tumour. When the lymphomas are obviously widely systemic and only incidentally involve the organ in their course, the problem does not appear to be under our immediate jurisdiction.

Lymphatic leukaemia.—The literature is indebted to Duanez and Castellanos¹⁵ for their collection of 100 cases of tumours of the thymus accompanied by leukaemia. Although the numerical breakdown is not made some of these have occurred as primary tumours with the blood picture altering secondarily. It is interesting to note that in their paper 55% of the cases occur under the age of thirty. This is significantly comparable to thymic sarcoma. The heavy male preponderance correlates nicely with the remainder of the thymomata. The disease as it affects the thymus runs an especially virulent and rapid course, the average duration being seven and one-half weeks.

The thymus was affected secondarily in several cases of myeloid leukaemia appearing at our hospital and our reported case falls into that category.

CASE 10

Clinical examination.—Male, S.M., aged 27 years, was admitted December 18, 1931, complaining of pain in the right chest and shortness of breath. Two months prior to admission he noted two enlarged right inguinal

nodes. These were followed by other nodular enlargements predominantly in the subcutaneous tissue of the abdomen. His chest pain and dyspnoea commenced one month prior to admission and two weeks later a non-productive cough developed. Weakness had become a late symptom.

On physical examination, enlarged bilateral epitrochlear, cervical and axillary nodes were found. The right chest was somewhat larger than the left and presented signs of a large amount of fluid with mediastinal displacement to the left. He had a remittent fever of 102.2° F.

Laboratory examination.—*Roentgen:* Evidence of a dense shadow obscuring the whole right lung which has displaced heart and other mediastinal contents to the left. *Pathological:* Bloody pleural fluid contained abundance of lymphocytes and a few myelocytes. Biopsy of skin nodule—leukaemia. *Hæmatological:* White blood count rose from admission value of 15,950 to 105,000 terminally. Differential on December 26, 1932, revealed: polymorphonuclears 7%; lymphocytes 55%; eosinophiles 7%; monocytes 5%; meta-myelocytes 1%; neut. myelocytes 8%; eos. myelocytes 8%; pre-myelocytes 9%. Red blood cells 5,040,000.

Clinical course.—Patient expired on February 10, 1932, following severe dyspnoea and cachexia.

PATHOLOGICAL SUMMARY

Gross findings.—Enlargement of the cervical, epitrochlear, and inguinal glands was present. Several subcutaneous nodules were found over the pectoral musculature.

There was a large tumour mass occupying the anterior mediastinum. This lay over the heart and was firmly attached posteriorly to the pericardium. This terminated above at the suprasternal notch and below at the diaphragm. It measured 26 by 3 by 2 cm. Laterally it invaded the upper and lower lobes of the right lung.

Of the abdominal organs, both the spleen and right kidney showed invasion by irregular islands of white, firm tumour.

Microscopical findings.—The main thoracic tumour and other sites show a diffuse cellular mass consisting of small round cells with little visible cytoplasm and a vesicular nucleus. Also present are large cells of the order of myelocytes with an eosinophilic granular cytoplasm. The bone marrow is typically that of myelogenous leukaemia.

Diagnosis.—Acute myelogenous leukaemia with multiple myeloid nodules in the skin, pleura, right lung, right kidney and myeloid metaplasia of spleen, liver, lymph nodes and a large thymoma of the myeloid type.

HODGKIN'S DISEASE

Mediastinal Hodgkin's disease has been known long and well by clinicians as an especially virulent and often times distinctly localized entity. Its rare occurrence in the thymus poses several interesting problems. If the theory is correct that Hodgkin's disease is a reticulo-endothelial neoplasia, where is its histogenic source of origin in the thymus? As far as is known a reticulo-endothelial tissue capable of giving rise to lymphoid elements is lacking in the thymus. The epithelial reticulum might be considered as an analogous entity but certainly not as identical in origin, function or characteristics.

From a morphological standpoint the thymic condition is not similar to the classical disease as described. The giant cells which occur are

much more numerous, hyperchromatic and pleomorphic. Reporters have consistently avoided designating them as Dorothy Reed or Sternberg cells.

There are two obvious alternatives to consider. One is that the more generally accepted theory regarding Hodgkin's disease is incorrect; the other is that one is dealing with a reticular cell tumour of a mixed cell nature and attended by fibrosis. Our case, although having the general features of Hodgkin's disease, is questioned on the basis of the typical giant cells.

CASE 11

An ambulance was called for the white male, E.M., aged 26, who was found to be in a precarious condition suffering from obstructive asphyxia. A tracheotomy was performed at once without affording relief since the obstruction was mediastinal. Cyanosis, dyspnoea, and pain increased until death occurred three days later.

PATHOLOGICAL SUMMARY

Gross findings.—Upon incising the skin and subcutaneous tissue over the sternum, a necrotic mass was found which extended through the sternum to become continuous with a mediastinal neoplasm weighing 2,000 gm. and measuring 20 by 11 by 13 cm. It occupied the entire superior and anterior mediastinum. It was greyish white in colour and firm in consistency. Behind, it enmeshed the trachea, came forward above and surrounded the arch of the aorta on the left and constricted the superior vena cava on the right. Laterally it ran over the hilum of the right lung and invaded the parenchyma for a distance of one centimetre.

The lymph nodes of the cervical region were enlarged and matted together as were those of the axilla. The larger mass of nodes measuring 2 cm. in diameter and section shows the same characteristics as the parent body. That is, the surface was a light grey in colour and broken by white strands of fibrous tissue. The nodes of the gastrohepatic omentum were likewise affected.

Microscopical findings.—Sections through the mediastinal mass show tumour arranged in lobules divided by fibrous tissue. Within the lobules there is a variable amount of diffuse connective tissue reticulum surrounding groups of cells and even individual cells.

The cell type varies a great deal. Some areas are composed almost entirely of lymphocytes while others contain an abundance of lymphocytes scattered throughout which there are many large polygonal cells. These are formed of moderate amounts of slightly eosinophilic cytoplasm and vesicular nuclei. Many of these larger cells are in mitotic division. A few reach giant dimensions and contain large hyperchromatic nuclei while others are multinucleated. Eosinophiles and polymorphonuclear leucocytes are present in considerable numbers.

No metastases are present in organs other than the cervical, axillary and gastro-hepatic lymph nodes. The bone marrow was not examined histologically.

Diagnosis.—Malignant thymoma of the Hodgkin's variety with metastases to the cervical, axillary and gastro-hepatic nodes.

SUMMARY

An endeavour has been made to outline the scope of the problem of malignant thymoma and to solve at least a few of the apparent conflicts which have made analysis so difficult, by:

1. Outlining briefly the histogenesis of the

thymus which makes it necessary to consider the organ and its neoplastic derivatives as arising from two cell systems; one lymphoid, the other epithelial.

2. Pointing out the extreme morphological similarity of the two systems in conditions of neoplasia.

3. Histopathologically, drawing the criteria of distinction between the main groups of thymic neoplasms.

4. Presenting cases illustrating the various types of malignant thymoma.

5. Systematizing their inter-relations and position in thymic oncology.

REFERENCES

1. GRANDHOMME, F.: Ueber Tumoren des vorderen Mediastinums und ihre Beziehungen zu der Thymusdrüse, Inaug. Diss., Heidelberg, 1900.
2. SYMMERS, D.: Tumours of thymic origin, *Ann. Surg.*, **95**: 544, 1933.
3. DECKER, H. R.: Primary malignant tumours of the thymus gland, *J. Thoracic Surg.*, **4**: 445, 1935.
4. EWING, J.: The thymus and its tumours, *Surg., Gyn. & Obst.*, **22**: 461, 1916.
5. COWDRY, E. V.: A Textbook of histology, Kingston, London, p. 132, 1934.
6. DANTCHAKOFF, V.: The differentiation of cells as a criterion for cell identification, considered in relation to the small cortical cells of the thymus, *J. Exper. Med.*, **24**: 87, 1916.
7. PAPPENHEIMER, A. M.: A contribution to the normal and pathological histology of the thymus gland, *J. Med. Research*, **22**: 1, 1910.
8. HAMMAR, J. A.: The new views as to the morphology of the thymus gland and their bearing on the problem of the function of the thymus, *Endocrinology*, **5**: 543, 1921.
9. MAXIMOW, A.: Untersuchungen uber Blut und Bindegewebe. II. Uber die Histogenese der Thymus bei Saugetieren, *Arch. f. mikr. Anat.*, **74**: 525, 1909.
10. BARTON, F. E. AND BRANCH, C. F.: *J. Am. M. Ass.*, **109**: 2044, 1937.
11. SLOAN, M. E.: The thymus and myasthenia gravis, *Surg.*, **13**: 154, 1943.
12. CROSBY, E. H.: Malignant tumours of the thymus gland, *Am. J. Cancer*, **2**: 461, 1932.
13. RUBASCHOW, S.: Eine bosartige Thymusgeschwulst, *Virchow's Arch. f. path. Anat.*, **206**: 141, 1911.
14. McDONALD, S. JR.: Reticulum cell carcinoma, *J. Path. & Bact.*, **35**: 1, 1932.
15. DUANEZ, P. AND CASTELLANOS, G.: Tumours of thymic region accompanied by acute leukæmia, *Arch. Cubanos Cancer*, **2**: 296, 1943; **3**: 40, 1944.

[Additional references may be had from the authors.]

It must be admitted that the evolution of plans for improvement in medical services on a local autonomy basis is discouragingly slow. It does not keep pace with advances in medical science or with improvements in technique of administration. But it must be remembered that the evolution of social structure under the principles of democratic government is a slow, tedious, discouraging, painful process. Yet, somehow, despite all its faults, we like it.—W. G. Smillie, *J. Am. M. Ass.*, **128**: 1005, 1945.