



ABSTRACTTUMORS OF PLEURA

Abstr. by Koucky.

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General:

Tumors of the pleura and adjacent structures have been described for a surprisingly long time. In spite of this, the literature on these tumors is still characterized by confusion in classification and terminology and by controversies regarding their nature. Clinically, there is a tendency to consider all such cases collectively as "intrathoracic tumors." The marked difference in prognosis of the various pathological types makes such a tendency undesirable.

Our Experience:

In the past year, 6 tumors in the pleura and adnexa have come to autopsy. The final diagnosis in these cases was as follows:

1. Endothelioma of pleura.
2. Endothelioma of pleura.
3. "Fibrosarcoma" of mediastinum.
4. Neurosarcoma (diaphragmatic region).
5. Sympatheticocytoma (9th D. ganglion).
6. Teratoma of mediastinum.

Each of these cases presented unusual diagnostic problems clinically and difficulty was encountered at autopsy in establishing a final diagnosis. In one case (fibrosarcoma of mediastinum), the diagnosis is still questionable. In 2 cases, the origin of the tumor is unknown. In addition, our experience illustrates the diversity of neoplasms found in this area and demonstrates the error of attempting to force all these types into 1 or 2 groups. Various authors apparently wish to describe these different tumors as phases or subgroups of 1 or 2 main types.

Historical:

1767 - Joseph Lietand - 2 cases (3000 necropsies).

1819 - Laennec - describes primary tumors of pleura.

1870 - 15 authors, in the intervening years have discussed these tumors.

In literature since 1870, many reports of various neoplasms of this region have been presented. In this material, 3 lines of work seem to be worthy of mention.

1. Robertson, H. E. (1924) - extensive summary and critical review of endothelioma of pleura.

2. Development of the picture produced by multiple fibromatosis in the thorax by Kienbock (1932).

3. Explanation of pathogenesis of neurosarcoma (Masson 1932) and of nerve ganglion tumors (Grieg, Wahl, etc.)

What little clarity there is today in the field of intrathoracic tumors is due chiefly to the work of these men.

Anatomy of Pleura:

The pleural spaces develop as slits within mesenchymal tissue independent of the epithelial elements of either ectoderm or entoderm. The lining cells became the flattened pavement type and are mesodermal in origin. This mesodermal tissue is capable of high differentiation (blood, bone, etc.) The pleural lining cells apparently possess a similar potentiality and the epithelial structures formed in some pleural neoplasms are explained on this basis.

In addition, other anatomical features, modify the nature of tumors in and about the pleura. In its immediate vicinity, there are large nerves and ganglia (vagus, sympathetic and intercostal); numerous lymph and blood channels; bone, muscle and cartilage. Also, several organs which were originally cervical (heart, diaphragm) migrate into the thorax carrying elements for the development of teratomatous tumors.

The anatomical divisions of the chest,

particularly the anterior and posterior mediastinum and the lateral pleura must be kept in mind. Certain tumors almost exclusively arise in each of these areas as will be discussed later.

Pathology:

On the basis of the literature abstracted for this meeting and also those previously presented (neurofibromatosis, neurosarcoma and neurocytoma), a working classification is attempted. No clarity can be obtained either in pathology or clinical pictures if genetically different tumors are grouped together. The following classification may prove inadequate as our knowledge progresses.

1. Incidental tumors.

Lipoma, chondroma, leiomyoma, Hodgkin's disease (also lymphosarcoma), etc.

2. Metastatic tumors.

(Note also extensions of multiple myeloma).

3. Developmental tumors.

Teratoma, dermoids.

4. Neurogenic.

Fibroma (all fibroma?), fibrosarcoma, myxosarcoma, myxofibrosarcoma, spindle cell, round cell sarcoma, neurocytoma, neuroblastoma, sympatheticocytoma, sympatheticoblastoma.

5. Endothelioma ("mesothelioma", carcinoma of pleura, etc.)

Group characteristics:

The location of the tumor is of importance. Almost without exception, teratomas and dermoids occur in the anterior mediastinum; neurogenic tumors in the posterior mediastinum and "endothelioma" on the lateral pleura. The metastatic tumors and incidental tumors may occur anywhere.

Incidental tumors: not uncommon. Lipomata frequent as fatty bodies along the intercostal spaces and over the diaphragm. Some become large enough to be of clinical significance. Chondromas are next in frequency. Hodgkin's disease of pleura is not rare and may be accompanied by "chylous" pleural effusion (Zon). The milky nature of the fluid is due to high protein content.

Metastatic tumors: would be of no particular significance except for the work of Robertson. He shows that a great number of so-called primary tumors of the pleura were in fact accompanied by a tumor elsewhere and were probably secondary growths. This work is quite convincing and therefore before any tumor is diagnosed as primary in the pleura search must be made for other possible primary lesions. Without actual statistical study of our own records, our experience in this respect is not as striking. Embolic Phenomena (petechiae, infarcts, tubercles, metastatic abscesses and tumors) are not frequently observed in the pleura.

Teratomas and demoids: have been previously reviewed. (Vol. 4, #3, Oct. 27, '32).

Neurogenic tumors:

Are greatest source of confusion. As previously stated in other meetings, neurogenic tumors are characterized by their extremely variable microscopic appearance. Various combinations of myxoid, fibrous and cellular (spindle cell, round cell, neural cell) elements are present. Many authors have tried to correlate these pictures with other types of thoracic tumors--the "endotheliomas" for instance. This adds to the confusion. Over 30 different names have been devised depending on the various combinations of cellular elements.

This confusion is somewhat surprising because the neurogenic group possess certain very definite characteristics. They are nearly all confined to the posterior mediastinum. Nearly all are accompanied by other findings of multiple fibromatosis which can be found if a search is made. Most of these tumors are localized, demarcated, cystoid in shape and show no metastasis. They range in size from

3 - 4 cm. to as large as a man's head. They project into the pleural space like a cyst. They grow slowly. On section, the interior varies from a firm, white fibrous structure to a soft gelatinous yellow material. Usually, they are attached only by a broad base. Erosion of bone and "hour-glass" formation through the intercostal spaces is not uncommon.

Malignancy is variable. The type described above is more common and corresponds to grades I to II. Grades III and IV are progressively more malignant. The type described above does not recur if entirely removed. The grade III infiltrates at the base and frequently recurs locally after excision. After operative interference, the malignancy sometimes increases. The grades IV are the most confusing. They infiltrate rapidly, the surface is no longer cystoid (encapsulated), the structure is very cellular, blood vessels are penetrated and numerous secondary deposits are found. A classification of pleural tumors sometimes used is localized and generalized. By the former is meant the fibrosarcomatous types, (neurogenic tumors, grade I to III of our classification) and by the latter is meant the endotheliomas. Obviously, grade IV neurogenic tumors are of this generalized type also. Moreover, endotheliomas in early stages may be localized (one of our cases).

Endotheliomas: are unusual tumors in many respects. They are soft nodular or cauliflower plaque-like or diffuse growths on the pleura. Probably all are localized at first (one of our cases) but they grow quickly and spread over the pleura either as a continuous tumor or else stud the pleura with innumerable secondary nodules (one of our cases). The visceral pleura frequently is spared. Effusion of bloody fluid into the pleural sac occurs and this collapses the lung by compression. Metastasis occurs in the hilar, cervical or axillary lymph nodes. Distant metastasis also occurs. Involvement of the opposite pleural cavity is found in some cases (one of our cases in a previous year).

Microscopically, the tumor usually contains only a relatively slight fibrous framework (contrast to neurogenic tumors). In some of the diffuse types, the fibrous reaction is more pronounced. The predominant cell is of an epithelioid type. It is large and each cell seems independent of the others (contrast to epithelial tumors of ectodermal or entodermal origin). Nests and strands are formed in an irregular manner. Keratinization and mucous production have been described (Robertson believes these are metastatic tumors). The tumors are very malignant and recur after attempts at removal.

The origin of the epithelioid cells is not understood. Two points of origin are offered. 1. Lining cells of the pleural sac; 2. endothelial cells of the lymph spaces. No significant data was found to confirm which of these 2 sites is the real point of origin.

Robertson in a long review of the entire subject came to the conclusion that "endotheliomas" of the pleura did not exist. It is his belief that in each case, the pleural growth is secondary to another primary focus. When such is not demonstrated, it is because the original tumor was small or was not looked for with sufficient care. The entire problem from a pathological aspect is still a very interesting controversy. Robertson's attitude is regarded very respectfully by most writers but is not entirely accepted. Ewing describes endothelioma of pleura as a tumor entity.

It should be noted that the material presented here is a general outline intended for use as a working basis. Even a hurried study of Robertson's work will show how extensive are the various controversies of diagnosis and pathogenesis of these tumors. The interpretation of the articles and the application of our own experience may have to be changed later.

The discussions as to the relative merits of the terms endothelioma, mesothelioma or carcinoma of pleura contribute nothing of note. No good data is presented to indicate dropping the simple term endothelioma in favor of another which may be more cumbersome or confusing.

### Clinical Features:

The clinical picture of endothelioma is linked with that of the other types of intrathoracic tumors (exclusive of lung).

On basis of symptoms, the clinical picture can be divided into two groups.

1. Asymptomatic.
2. Symptomatic.

A surprising number of cases are discovered accidentally. (Kienbock) Routine physical or roentgenographic examination shows the presence of an unsuspected mass (one of our cases). Usually these cases are the grade I or II neurogenic tumors or else benign incidental ones.

The clinical picture is outlined by Cripp most concisely. The age ranges from 20 to 40. Males preponderate. The right side is involved more frequently than the left. The onset is insidious and the course progressive. In the beginning, there is a slight cough and a deep dull pain in the chest. Later sputum is raised. Later, there are signs of cachexia and toxemia. The course is usually afebrile. On physical examination, retraction, lagging, dullness, decreased fremitus and absent breath sounds are found. Fluid is usually present. Secondary anemia is commonly found. The axillary or cervical nodes may be involved and microscopically the nodes show atypical malignant tissue. The fluid is of the transudate type and is hemorrhagic. The cytology (Robertson) of the aspirated fluid "shows the usual elements of the blood, and, in addition, varying numbers of large swollen cells singly, or in clumps or small plaques." Diagnoses of malignancy have been made by study of the puncture fluid. This is possible when there has been a fortunate aspiration of a cellular plaque large enough for adequate study. These symptoms and signs are equally applicable to endothelioma or to malignant neurogenic tumors. Some tumors give rise to special findings when peculiar--

ly located,--compression of a single bronchus for example.

### Roentgenographic Aspects:

The high degree of accuracy reached by roentgenologists in other types of tumors is not possible in pleural tumors. Adhesions, thick pleura, pleural effusions, atelectatic lung parenchyma all contribute to mask the true findings.

The round cystoid neurogenic tumors frequently given excellent roentgenographic findings. These tumors usually are not accompanied by pleural effusion. Kienbock feels that these tumors should be diagnosed with accuracy.

Pneumothorax as a procedure preparatory to roentgenoscopy has proven valuable. The separation by air of the lung and mediastinum from the parietes allows adequate study of the pleura. Accurate diagnosis and estimates of position and size can be made. This procedure, however, can become dangerous. Collapse of a lung in the presence of an already burdened circulatory system may give rise to unexpected symptoms.

Removal of fluid is necessary to decrease the density of the thorax and to allow the introduction of air. This removal produces the greatest number of complications. The intrapleural pressure in cases of effusion is positive (below the fluid level). The lung has been collapsed for a prolonged period by the effusion. Withdrawal of the fluid changes the intrapleural pressure to a high negative pressure. The lung usually does not reexpand enough after prolonged compression to fill the space set free by the withdrawal of the fluid. The high negative pressure produces an acute pulmonary edema (the high negative pressure acts as a suction pump on the lung capillaries). This accident has occurred in our experience in at least 2 cases. Injection of air to correct the unnatural pressure relieves the condition. If care is taken to keep the intrathoracic pressure within -4 to -10 cm. water, the aspiration of the pleural effusion and injection of air causes no distressing symptoms.

### Diagnosis:

Stigmata of multiple fibromatosis, location in the posterior mediastinum and the cystoid shape of the tumor will aid in the diagnosis of a great many of the neurogenic tumors.

Location in the anterior mediastinum is extremely indicative of teratomatous growths. A location to the lateral pleura almost limits the diagnosis to endothelioma and incidental tumors (or metastatic tumor).

Examination of puncture fluid is not of as great value as is generally thought. The presence of blood is suggestive but not diagnostic even of malignancy. The value of the cytology of the fluid is accidental. Some examinations demonstrate malignant masses. (In our experience, the method has not been encouraging. In one case of mucoid carcinomatosis of the peritoneum, tumor cells were recognized after the diagnosis was known through other means. Studies of fluids from cases with Hodgkin's disease, leukemia and even cardiac ascites have shown sediments similar to those from proven malignancy.)

The differential diagnosis includes tuberculous pleurisy, encapsulated effusion or empyema, tumor of lung, Hodgkin's disease, aneurysms, paravertebral abscess, myeloma and others. Inflammatory conditions are the usual diagnoses.

### Treatment:

Surgical removal of tumors of the pleura or mediastinum is not as hopeless as it might seem. Very careful technique of preoperative treatment (pneumothorax and others) anesthesia and postoperative care have been developed which have made this branch of surgery practical and successful.

Because of the limitations in the extent of the resection possibly due to the proximity of the vital organs,

it appears an almost unavoidable conclusion that only moderate sized benign tumors or those of low malignancy can be removed. Incidental tumors (lipomas, chondromas) teratomas, dermoids and grade I to II neurogenic tumors can be removed with good prognosis. This emphasizes the need for a working classification and good diagnosis.

In Harrington's experience, all the endotheliomas died within a short time.

The status of surgical removal of intrathoracic tumors is illustrated by Harrington's experience. His cases included all types and some were very large (i.e., not a picked group).

1931 (Feb.)

<u>Malignant</u>	14
operative deaths	1
subsequent deaths	9
living	4
<u>Benign</u>	14
operative deaths	2
living, asymptomatic	12

1931 (Sept.)

33 cases, 4 operative deaths.

Harrington believes that exploration is warranted whenever there is an indication of a benign or low grade malignant lesion.

#### Summary:

1. Pleural tumors have been recognized for nearly 200 years.

2. Our own experience with 6 cases in one year indicates that such tumors are not infrequent.

3. In spite of the long period of study, the literature is characterized by marked controversies regarding the classification and nature of the tumors.

4. Development in our knowledge of neurogenic tumors within recent years has clarified the problem somewhat.

5. The pleura is developed from mesenchymatous tissue which in its primitive state has a marked power of differentiation.

6. Adjacent structures such as nerves may produce tumors closely associated with the pleura.

7. A possible working classification divides the pleural tumors into (a) incidental tumors such as lipomas, chondromas, etc., (b) metastatic tumors, (c) developmental tumors (teratomas), (d) neurogenic tumors which include all the gradations of the fibrosarcoma group and (e) endotheliomas.

8. The location of the tumor is a very important feature. The typical tumor of the anterior mediastinum is the teratoma; of the posterior mediastinum, the neurogenic tumor; of the lateral pleura, the endothelioma.

9. Incidental tumors of the pleura are not uncommon.

10. Metastatic tumors must be constantly kept in mind because some so-called primary pleural tumors may be really metastatic.

11. Neurogenic tumors are characterized by the extremely variable microscopic appearance. They include perhaps all the fibroma-fibrosarcoma type of tumor in addition to the nerve cell types. The more benign types are characterized by their local, encapsulated nature. The very malignant ones are confusing because of the extensive spread.

12. Endotheliomas are carcinoma-like growths which are peculiar because of the frequent diffuse involvement. They may be localized however. The chief cell is epithelioid, the origin of which is unknown.

13. In spite of the various controversies, there is no good evidence for dropping the term endothelioma.

14. Many pleural tumors are entirely asymptomatic. In the remainder, the symptoms and findings are not specific.

15. The malignant tumors are accompanied by hemorrhagic effusion.

16. Pneumothorax as an aid to roentgenography is valuable but care must be taken to maintain a normal pleural pressure in such procedures.

17. The diagnosis is suggested by the position of the tumor and by stigmata of multiple fibromatosis elsewhere in cases of neurogenic tumors.

18. Chronic inflammatory processes pleural tumor.

19. Surgical removal is hopeful in cases of benign or low grade malignant tumors and hopeless in the remainder.

## II. CASE REPORT

### ENDOTHELIOMA OF PLEURA? (DIFFUSE TYPE)

Path. Koucky.

Case is white male, 50 years of age, admitted to Minnesota General Hospital 8-5-32, expired 8-8-32 (4 days).

#### Weakness, weight loss, cough.

12-1-31 - Began to feel weak and lost weight.

1- -32 - Developed cough which persisted, (not productive). Sputum not blood-tinged. Difficulty in sleeping and continued very tired.

4- -32 - Stopped work because of symptoms. Lost about 15 lbs. in weight since onset of illness.

#### Effusion, Diagnosis of Tbc.

5- -32 - Developed dyspnea, which increased in severity, only relieved by lying on right side. At this time, was admitted to an outside hospital. Thoracentesis done and considerable amount of dark colored fluid drawn from left chest. Diagnosis of pulmonary tuberculosis is made. Referred to sanatorium. At sanatorium chest tapped 6 times and bloody fluid withdrawn. Liver began to enlarge, axillary glands became apparent and small nodules developed beneath skin of chest. It was thought that patient was not suffering from tuberculosis but probably had malignancy and was referred to Minnesota General Hospital for diagnosis.

#### Admitted, emaciation, carcinomatosis, pleural effusion.

8-5-32 - Admitted. Physical examination reveals emaciated, white male with breathing labored. Prefers to lie on left side. Neck - several hard, shotty glands in all triangles. Chest - several small, hard, subcutaneous nodules on anterior surface; left side dull throughout; no breath sounds heard; heart - impulse not felt and percussion difficult because of dullness in left chest, sound, rate and rhythm normal,

blood pressure 125/90. Abdomen - liver palpable 2 fingers below costal margin, smooth and not tender. Extremities - negative. Rectal - definite rectal shelf. Laboratory: Blood - Hb. 74%, wbc's 11, 600, rbc's 4,500,000, P 87%, L 13%. Progress: During 3 days stay, temperature ranged from normal to 100. Pulse elevated, 100 - 140. Respirations about normal.

#### Biopsy: unusual epithelioid tumor.

8-6-32 - Biopsy of cervical node shows carcinomatous metastases, probably squamous cell type which appears highly malignant. Thoracentesis - 1500 cc. bloody fluid. Very dyspneic. X-ray of chest - Massive hydropneumothorax shown in left chest obliterating practically entire left chest. Heart and mediastinum pushed over to right. Some evidence of congestion in right chest, but no other change. Conclusions - Hydropneumothorax left lung, with displacement of mediastinum.

#### Pain in chest.

8-7-32 - No change. Dyspneic. Difficulty in moving about. Complains of pain in chest.

#### Sudden Exitus.

8-8-32 - More dyspneic. Thoracentesis - 200 cc. bloody fluid. P.M. - Much weaker and more dyspneic. Respirations labored. Expired suddenly at 2:05 P.M.

#### Autopsy.

Emaciation, subcutaneous metastasis.  
Body is greatly emaciated but well-developed, white male, 50 years old, measuring 160 cm. in length, weighing approximately 115 lbs. Rigor beginning. Hypostasis purplish and posterior. Minimal amount of edema in lower extremities. Marked cyanosis over upper part of body. No jaundice. Pupils equal, measuring 6 mm. in diameter. Puncture wounds from thoracenteses on left side of chest. Palpation of anterior chest wall shows small, hard nodules described under physical examination. Palpation in cervical and axillary regions reveals several hard nodules. Inguinal glands appear enlarged and hard, although enlargement not marked.

Peritoneal Cavity shows peritoneal

implant in culdesac behind prostate (rectal shelf). Appendix atrophic.

Hemorrhagic pleural effusion.

Right Pleural Cavity appears normal. Left completely filled with fluid. Fluid bloody but does not appear inflammatory in nature. Some fibrin and blood clots present but no pus. Pericardial Sac normal. Heart 275 gms. No changes.

Right Lung weighs 375 grams, Left 950. Right lung fully expanded. Through substance of this lung are several small, hard, shotty nodules. Largest measure about 1 cm. in diameter. On cross section, all nodules are definitely malignant. Between 15 and 20 such nodules are seen in lung substance. Left lung completely and uniformly collapsed against mediastinum. Size of lung is such that it displaces about 250 cc. of water. Mediastinum approximately in midline. Entire left chest has been filled with fluid as described above.

Parietal and visceral pleurae remarkably thickened, measuring from 2 to 5 mm. in thickness. It can be stripped from the chest wall quite easily but leaves a ragged surface, indicating that penetration through the parieties has taken place. Anterior chest wall has been infiltrated so that the interspaces and subcutaneous tissue contains numerous, 4 or 5 mm. sized, white nodules.

Diaphragm on left side completely transformed into same leathery type of tissue. Abdominal surface of diaphragm shows numerous sessile tumor nodules. Left side of pericardium infiltrated in same manner and heart side of pericardium shows some projections. Visceral pericardium, however, is not invaded and opposite side of pericardial sac is thin and normal.

Pleura is universally involved on parietal side. Visceral pleura of lung appears entirely uninvolved. It is covered by heavy layers of fibrin and some blood clots, but no malignant tissue is apparent in this portion of pleura. Lung is opened along bronchi. Definite malignant tissue at hilus of lung adjacent to mediastinum, but this appears to be an extension into the lung along the bronchi rather than primary focus of the lung. Bronchial mucosa intact throughout

all bronchi which could be opened. Some difficulty encountered in opening smaller bronchi because of completely collapsed condition. Lung parenchyma on this side appears entirely uninvolved by malignancy. No nodules found. Lung parenchyma quite friable. Mediastinum infiltrated by tumor tissue which appears to be both extension from parietal pleura and numerous metastatic lymph nodes. No compression of bronchi apparent. It appears that the collapse of left lung is due to fluid in pleural space rather than collapse from compression of bronchi.

Metastasis, no other primary focus.

Spleen 175 grams. Upper pole somewhat adherent to diaphragm. No metastases found.

Liver 1600 grams, contains innumerable nodules ranging in size from 5 mm. down to those just visible. Nodules are spread irregularly through the liver appearing on the surface and within liver substance. One of larger masses is necrotic in center and liquefied.

Gall-Bladder and bile ducts appear normal.

Gastro-Intestinal tract: There is a metastatic nodule in wall of stomach which appears on serous surface and projects under mucosa but mucosa is intact over nodule. No evidence of primary focus in gastro-intestinal tract.

Pancreas contains several metastatic nodules. No evidence of primary focus.

Adrenals are normal.

Left Kidney 180 grams, Right 220, are large, swollen and red. No other disease.

Bladder appears normal.

Prostate is small and has no suspicious areas within it.

Aorta is normal.

Generalized involvement present of all Lymph Nodes extending down to bifurcation of aorta.

Nodes along abdominal aorta measure up to 2.5 and 3.0 cm. in diameter.

Neck. Thyroid appears slightly large, although uniform in consistence. No evidence of primary focus. Esophagus normal.

Head. Not examined.

Diagnoses:

1. Primary endothelioma of left pleura (diffuse type).
2. Collapse of left lung.
3. Pleural effusion.
4. Metastases to cervical and axillary nodes, mediastinal and abdominal lymph nodes, lungs, thoracic wall, liver, diaphragm and peritoneum, stomach wall and pancreas.
5. Cloudy swelling of kidneys.
6. Emaciation.

Microscopic:

The framework of this tumor is heavy fibrous tissue. In this are numerous sheets and cords of malignant cells. The cells are arranged in layers much like squamous epithelium. The cytoplasm is abundant, the nuclei are large and finely granular. Cell outlines are usually distinct. All the metastasis have the same construction.

Comment: Because of the heavy fibrous tissue reaction and the tendency of the cells to arrange themselves into squamous and epithelial-like structures, the diagnosis of endothelioma can be questioned. Because of the presence of nodules in the lung parenchyma, the possibility of a primary lesion in lung cannot be ruled out.

Conclusion: Possible endothelioma of pleura.

III. CASE REPORTENDOTHELIOOMA OF PLEURA.

Path. Koucky.

Case is adult, white male, 45 years old, admitted to Minnesota General Hospital 5-9-32, expired 7-8-32 (60 days).

Pain

2- -31 - Quite suddenly developed sharp pain in left shoulder, did not radiate, but was limited and could be localized with one finger.

3- -31 - Pain persists but is growing worse. Dentist consulted with idea that teeth might be cause of pain. Teeth extracted. No improvement.

10- -31 - Went to mud bath sanatorium without deriving any benefit. Pain in shoulder becoming worse, in fact so severe that patient cannot eat or sleep and in general feels very miserable. Now taking capsules to relieve pain.

Pain marked

2- -32 - Pain now so severe that patient is unable to sleep in bed but has to sleep sitting in a chair. Pain aggravated on lying down.

4- -32 - Edema of legs begins, starting in right leg and later in left. Unable to wear shoes.

Swelling of left hand, pleurisy pain.

5- -32 - Left hand began to swell and this is accompanied by burning sensation. Pain like that when the "crazy bone" is struck. Developed pleuritic pains in left chest.

Family history

Father died at 56, of heart trouble. Mother living and well at 70. 8 siblings living and well, 1 died of unknown cause.

Past history

Pneumonia at 7 and rheumatism 3 years prior to admission. Past health otherwise excellent up to onset of present illness.

Admitted

5-9-32 - Symptoms focus on left shoulder and neck. Some blurring of vision. Occasionally has catarrh and colds. Nocturia about 4 times a night. Drinks great deal of water which causes polyuria. Physical examination: Appears to have lost weight. Pain while lying in bed. Eyes - left pupil constricted and does not react to light or accommodations; ptosis of left eyelid. Chest - decreased resonance over left apex; breath sounds slightly diminished; drooping of left shoulder; otherwise no definite findings. Heart - blood pressure 112/60; loud, blowing systolic murmur at apex which does not seem to be transmitted; heart does not appear to be enlarged. Abdomen - negative. Skin - brownish pigmentation over back and left chest. Extremities - edema of left arm and

both legs up to knees; pain on motion of left shoulder joint. Back - slight scoliosis to right in mid-dorsal region; left scapula appears enlarged as though there is a mass behind (hard, immovable and tender). Rectal - negative. Laboratory: Urine - few hyaline casts, few rbc's, trace of albumen, specific gravity 1.023. Blood - Hb. 72%, rbc's 3,310,000, wbc's 11,000, pmn's 66%, L 34%. N.P.N. - 30.08, calcium - 10.266.

Tumor left shoulder, no other focus.

X-ray of chest, heart and abdomen - Both kidneys within normal limits in size, shape and position. No evidence of disease in urinary tract. Heart well within normal limits in size, shape and position. Large density over left apex, suggesting soft tissue mass, and very definite erosion of posterior portion of 2nd rib just at articulation with spine. Some thinning of 1st rib in same area. Appearance suggests tumor of rib with secondary involvement of pleura or endothelioma of pleura with secondary involvement of rib. Scapula appears entirely normal. No other evidence of disease. Conclusions: Probable sarcoma of 2nd rib. Possible endothelioma of pleura with secondary erosion of rib.

Films

Of both shoulders lower cervical and upper dorsal spine and ribs. Marked destruction of posterior portion of 1st and 2nd ribs, especially 1st, extends anteriorly to some degree. Large soft tissue mass about this. Some suggestion of invasion of transverse processes of 1st and 2nd thoracic vertebra, although this is not entirely definite. There may be slight erosion of posterior end of 3rd rib. Both scapulae and shoulders appear quite normal. Slight thinning of outer margin of left scapula, which suggests pressure process rather than primary lesion in scapula itself. X-ray of gastro-intestinal tract - fluoroscopic examination of stomach shows no evidence of gastric disease.

5-12-32 - Examination of mass shows it to be tender, tense, filling out intraspinous fossa of left scapula. Feels somewhat fluctuant. Needling of mass yields only a little blood.

Clinical impressions

5-16-32 - Staff rounds - diagnoses considered. Chief of Medical Service - carcinoma of lung. Chief of Surgical Service - neurofibrosarcoma. Chief of Roentgenology Service - endothelioma of pleura. Others - lesion originating in region of scapula, penetrating into chest secondarily.

Biopsy - no help

5-27-32 - Biopsy of infraspinatus muscle taken - shows muscle fibers to be separated by a few cells appearing like fibroblasts. Fibers are pale staining. No conclusions. Tentative diagnosis - fibrosis of muscle. Aspiration of mass - yields blood, a few leucocytes and an occasional round cell of unknown origin.

X-ray

6-2-32 - X-ray of spine, left scapula - findings in upper left ribs and pleura about same as last reported. Cervical spine shows considerable distortion probably due to change in ribs, but distortion is so marked that definite metastases cannot be made out. Distinct nodular area of lessened density in body of 4th thoracic vertebra which strongly suggests one local metastasis. All thoracic and lumbar vertebrae show lack of detail, the trabeculations apparently having disappeared. This is very uniform and suggests marked osteoporosis which may be due to very diffuse metastasis. Marked calcification of aorta beginning about 5 cm. below arch at very sharp point and extending right down into abdominal aorta and involving iliac arteries. Most extreme calcification and rather unusual for individual of this age.

Femoral thrombosis.

6-14-32 - Thrombosis of left femoral vein and edema of left leg. Dry heat applied. Gradually losing strength. Since admission, temperature has shown almost daily rises up to 101.5.

Worse, progressive anemia, terminal pulmonary complications.

7-6-32 - Definitely worse. Has been

gradually losing weight and strength. Confined to bed most of time. Respiration to 40 and are labored. Temperature 101. Semi-comatose and responds to questions poorly. Dullness present throughout entire left chest with retraction of left apex. Rales and bronchial breathing in left lung posteriorly. Pneumonia of left lower lobe considered.

Repeated urine examinations show only occasional wbc's or negative urine. Hemoglobin has slowly fallen so that now it is only 40%, wbc's range from 6,000 to 8,000. Electrocardiogram - sinus tachycardia.

Clinical impression: No further changes in diagnosis. Terminal pneumonia.

### Autopsy:

#### Emaciation

Body is well-developed but poorly nourished, white male, 45 years of age, measuring 168 cm. in length and weighing approximately 110 lbs. Rigor absent. Hypostasis just beginning. Edema of both legs extending up to knees and some swelling of left arm. No cyanosis or jaundice. Pupils equal, measuring 3 mm. in diameter. Two hemangiomas of right forearm. No lymphadenopathy made out. Contour of chest, anteriorly, appears normal. Biopsy incision over left scapula. Slight fullness in subscapular space on left side.

Peritoneal Cavity is dry. Appendix small and cord-like.

Left Pleural Cavity contains from 700 to 900 cc. purulent material. Upper portion completely obliterated. Right pleural cavity normal. Pericardial Sac contains definite excess of clear, straw-colored fluid.

#### Arteriosclerosis, rheumatic endocarditis.

Heart 290 grams. Heart muscle soft and somewhat pale. Pulmonary valves intact. Mitral valve, particularly aortic leaflet, is short because of ridge of thickening along its edge. The aortic valves contain a few atheromatous plaques near their base. Coronaries normal.

The Root of the Aorta: About 1.0 cm. above the valves, there is an atheromatous plaque about 1 x 1.5 cm.

Right Lung 450 grams, Left 750. Right

lung very emphysematous and light, its bronchi contain an excess of mucus in the main division. Parenchyma shows no disease.

#### Tumor, abscesses.

Left Lung is almost entirely collapsed. Only anterior and lower portions of the upper lobe are air-containing. Lower lobe is entirely atelectatic as well as the posterior and upper parts of the upper lobe. The apex of the left lung is attached to the pleura at the posterior portion opposite the 1st and 2nd ribs. It tears away readily, leaving a raw, friable surface on the pleura and on the lung. Sectioning through the lung shows the entire lung to be fleshy in consistence, being speckled throughout by various yellowish spots from which pus can be expressed. In 5 or 6 areas in the lower lobe, these spots are much larger and measure up to 1.5 cm.--from these, several drops of thin, brownish pus can be expressed. Most of these areas are subpleural, whereas the small white spots involve the entire lung tissue. The mass in the apex is entirely subpleural and appears to be extension from the parietal pleura into the lung rather than a tumor within the lung itself. The mass consists of a plaque about 3 cm. in diameter and about 1.0 cm. in depth. This is friable, soft and has a yellow color. The edge of this tumor is convex and points into the lung. The lung about the tumor mass is the seat of the same type of purulent white spots.

#### No other primary focus?

The Spleen (100 grams), Liver (1950 grams), Gall-Bladder, Pancreas, Adrenals, Bladder and Prostate normal.

Gastro-intestinal tract shows 5 or 6 diverticulae. No evidence of tumor.

Each of the Kidneys weigh 150 grams. The left kidney shows a few old, healed infarcts. Otherwise no other gross pathology is made out.

#### Arteriosclerotic aorta.

There is a very marked longitudinal plaque of calcification within the Aorta beginning at the arch and extending to and into the abdominal aorta. This feels like a broad sliver of bone

within the aorta itself.

Lymph Nodes not enlarged within the abdomen and mesentery. In the hilus of the left lung, there are a few moderate size hyperplastic nodes and another can be palpated behind the bifurcation of the trachea.

#### Tumor

Organs of Neck, Ribs and Tumor. Dissection of left side of neck, left ribs and vertebrae carried out. Tumor mass described in apex of left lung apparently is a continuation of a tumor arising in region of posterior part of 1st rib. Pleural surface over this rib shows a cauliflower-shaped tumor, measuring 5 x 6.5 cm. Edge of tumor is serpiginous and heaped up like edge of an ulcerating malignancy. Tumor stands up above surface of pleura for a distance of 3/4 cm. Neck and angle of 1st rib entirely replaced by tumor tissue. Rib can be bent and moved about at this point.

Dissection of neck shows that tumor has infiltrated into insertion of scalenus muscles and transforms them into a mass of muscle and tumor. Brachial plexus at its origin in between scalenus muscles is normal. At a point in brachial plexus where median cord passes around subclavian artery, tumor mass has infiltrated lower head of median nerve. This appears to be only point of attachment to brachial plexus. Subclavian vein penetrates through tumor but does not appear entirely obstructed. Tumor in this area in scalenus muscles and opposite brachial plexus is firm, yellowish, gelatinous and fibrous structure without any outline. It has eroded vertebra opposite 1st and 2nd ribs. Appears to have infiltrated foramina for nerve roots.

Interspace between ribs is involved by tumor tissue. 2nd rib intact and cannot be moved about but tumor tissue is immediately adjacent to this rib and may be eroding it. Cervical tissue along carotid artery and above tumor mass shows few pinhead size, soft lymph nodes which do not appear involved by malignancy. Infra-supraspinatus fossae are exposed. Muscle here is pale and somewhat gelatinous but no definite tumor can be made out. Subscapular space is explored and muscle in this area shows same characteristics without any definite tumor infiltration. Brain and spinal cord not examined.

#### Diagnoses:

1. Pleural endothelioma.
2. Penetration of brachial plexus, of 1st and 2nd ribs, of 1st and 2nd vertebrae, of pleura, of lungs and of scalene muscles.
3. Multiple lung abscesses, left lung.
4. Secondary atelectasis of left lung.
5. Empyema, left.
6. Hydropericardium.
7. Emphysema, right lung.
8. Old rheumatic endocarditis, mitral valve (?).
9. Myocardial cloudy swelling.
10. Calcification of aorta, extreme.
11. Hemangioma of left arm.
12. Obstruction of subclavian vein, left.
13. Edema of lower extremities.
14. Diverticulae of colon.
15. Emaciation.

#### Microscopic:

Stroma consists of a light framework of fibrous tissue in which are masses of tumor cells and areas of necrosis. The tumor cells are large and polymorphous but tend toward a round shape. Each is distinct and independent of adjacent cells. No tendency toward glandular or epithelium-like structures. The nuclei are large and relatively poor in chromatin. No pigmentation found in other organs.

The muscle of the subscapular area shows no tumor.

#### Conclusion:

Primary endothelioma of pleura.

#### IV. SUMMARY OF INTRATHORACIC TUMORS AT MINNESOTA GENERAL HOSPITAL 1932 - 33.

1. "Fibrosarcoma" of mediastinum (?), Inflammatory granuloma (?).  
G.H. - age 3, expired 2-15-32.  
Oct. '31 - Fullness in throat after meals.  
Nov. '31 - Diagnosis of cardiospasm.  
Dec. '31 - Regurgitating all foods.  
1-7-32 - Admitted. Past history: Pneumonia at age 1. (Significance?)  
Examination - dehydrated, emaciated, vague findings in chest. X-ray:

2 structures of esophagus. Course: gastrostomy and other therapy. Child expired with respiratory difficulty.

Autopsy: Solid mass of upper pleural cavity (left) and posterior mediastinum (hard, white, infiltrating tissue.) Stricture of left bronchi and collapse of left lung. Nodular masses above diaphragm. Microscopic: infiltrating fibrous tissue. Diagnoses: Chronic inflammatory granuloma (?), Neurosarcoma (?), Fibrosarcoma of unknown source (?).

2. Teratoma of chest (previously reviewed).

F. P. - age 16, expired 6-8-32.

Sept. '31 - Pain in chest.

Dec. '31 - Cough.

Jan. '32 - Chest tapped, fluid obtained, rib resected.

Mar. '32 - Another rib resection.

May '32 - Pain, cough continue. Night sweats (due to secondary empyema?).

5-26-32 - Admitted. Fungoid growth through operative wound. Entire right chest flat.

X-ray - appearance of massive effusion.

Course: 6-5-32 - Operated. Massive tumor found.

Autopsy:- Massive teratoma of anterior mediastinum growing into right side of chest.

3. A. W. - reviewed today.

4. F. G. - reviewed today.

5. P. K. - reviewed previously.

Age 56. Expired 10-31-32.

Oct. '30 - Fracture of ribs (left).

May '32 - Intermittent pain since. Injured again.

Aug. '32 - Pain, weakness, loss of weight. Pain radiates along intercostal nerves.

9-7-32 - Admitted. Past and family history: 1 child with malformed

chest. Had partial resection of stomach 1916 (reason unknown). Examination:

Multiple subcutaneous nodules otherwise no significant findings. Biopsy of skin nodules - "neurofibroma". X-ray: osteoporosis of bones. Course: Progressive decline. Mass developed in left upper quadrant. Hemorrhagic fluid in chest.

Autopsy: Extensive tumor of diaphragm and

chest wall with metastasis to numerous viscerae. Diagnosis: neurosarcoma (grade IV), neurofibromatosis.

6. J. T. - age 78, expired 1-9-33.

Oct. '32 - Pleurisy, left.

Dec. '32 - Gall-bladder symptoms.

Past history: 20 years prior - "fibroma" of scapular region removed.

1-4-33 - Admitted for gall-bladder disease. Examination negative except for subcutaneous tumor, left axilla. X-ray: tumor eroding 9th dorsal vertebra on right side. (Incidental finding.) Clinical impression: Endothelioma of pleura, myeloma, metastatic carcinoma. Expired from pneumonia.

Autopsy: Pneumonia, chronic gall-bladder disease, tumor of 9th dorsal sympathetic ganglion with erosion of vertebra. Microscopic: ganglion cell tumor.

Diagnosis: Sympatheticocytoma.

## V. NEWS

### 1. Women Try - Men Do:

A Thousand Cases of Attempted Suicide.

F. C. Lendrum, M.D.: Suicide causes more deaths in the United States than puerperal sepsis, duodenal ulcer, Hodgkin's disease, leukemia, scarlet fever, and acute anterior poliomyelitis taken together; yet it has received comparatively little study.

### Material

An analysis is presented of a thousand cases in which patients were admitted to the wards of the City of Detroit Hospital in the years from 1927 to 1930, because of attempt at suicide. This group is not entirely representative of the whole class of patients who attempt suicide, especially on account of the absence of patients who used rapidly fatal agents, and on account of the relative infrequency with

which wealthy patients are brought to the hospital.

### Sex

The group consisted of 363 males and 637 females. Of the seventy-two patients who died, however, forty-one were males and thirty-one females. In the United States as a whole, moreover, there are three deaths from suicide among males to one among females. These facts confirm the general view that females are more likely to attempt suicide than males, but much less likely to be successful.

### Age

The distribution curve by age showed, among females, a conspicuous peak between the ages of twenty and twenty-four years, and very few cases after the age of the menopause. Among males the peak of the curve was not so conspicuous and came later, between the ages of twenty-five and twenty-nine years. In males there is very little decline in the rate of suicide with advancing years.

### Race - Marital Status

Negroes made a relatively larger number of attempts at suicide, and a smaller number of successes, than white people.

As to marital distribution, the group studied was not significantly different from the general population except that the former group contained a larger proportion of divorced women.

### Religion

The data appeared to indicate a relatively much greater incidence of attempted suicide among Protestants than among Catholics. However, a comparison of the religious preferences of these patients with the number of members claimed by the various denominations in the Religious Census of 1926 is likely to be very unreliable.

### Occupation

The percentage of unemployment among the gainful workers of the series studied was significantly greater than in the

general population. A comparison, however, of the national suicide-rate with the annual stock market averages failed to reveal any evidence of relationship between them. The data were not sufficiently complete to allow a statement as to the effect of occupation on the incidence of attempts at suicide. The common view, however, that the incidence of suicide is higher in the professional than in the laboring classes is probably founded on a misinterpretation of statistics. Among physicians, for example, the apparent high rate of suicide disappears when corrections have been made for the distribution by age and sex of the members of the profession.

### Time

Attempts at suicide were relatively rare in the early morning and most frequent in the evening. They were also relatively rare in the middle of the week, and most frequent near the week-end, especially on Sunday and Monday.

### Motive

The leading motives assigned for the attempt by male patients were economic difficulties, and by female patients, marital, amatory, or domestic discord. Eighty-eight patients attempted suicide because of ill health, in most cases because of chronic, harassing pain, of which epigastric pain of men and pelvic pain of women were the leading forms.

### Disease

Twenty-three per cent of the patients received some psychiatric diagnosis, which in a little more than half of the cases was some form of acute or chronic alcoholism. The large number of cases of drug addiction also deserves mention.

Serologic tests for syphilis were completed on nearly half of the patients and surprisingly, there was a much higher proportion of positive results among females.

Manner

Poisoning was employed by both sexes as the leading means of attempt at suicide, and was used by 75 per cent of the patients. The relatively greater preference of males for mechanical methods, however, largely accounts for the greater number of successes among males. The most common poison, tincture of iodine, was used by 268 patients without a single death. It was followed, in order of popularity, by the much more dangerous solution of cresol (lysol), mercuric chloride, and phenol.

Prognosis

More than 85 per cent of the patients were released to their relatives or dismissed as well. Of patients so released, it can be assumed that only a relatively small number ever made another attempt on their lives. This assumption is based on the knowledge that only about 2 per cent of the 1000 patients studied had ever made a previous attempt.

From: Proc. Staff Meet. of Mayo Clinic, 8:179-180, (Mar. 22) '33.

2. Should We Tell?

Our policy is to tell cancer patients if they ask, on the assumption they would not ask if they did not want to know. To lie would be confusing. Relatives and friends knowing of our deception would not believe other physicians if they consulted them about their own condition, suspecting cancer. It has been said that our patients are "different"-- I wonder. The gory details can be omitted and certainly no intelligent physician ever goes "psychic" and predicts the outcome in so many months or years. The following item from the Budapest letter (J.A.M.A. 100:1052 (Apr. 1) '33 is of interest.

"Dr. Imre Basch, late director of the St. Stephen Hospital in Budapest, became ill some months ago with pain in his chest and difficult breathing. His physician friends assured him that his condition was not grave. He felt that his friends concealed the truth, and he tried a pious

fraud. He wrote to Professor Finsterer in Vienna that a patient of his would call on him, whom he suspected to have cancer. He called on the professor, giving a false name. Finsterer made a thorough examination and said that he would give instructions as to treatment to his attending physician, Professor Basch of Budapest. In this letter he reported that his patient had cancer of the lungs and in his opinion had about two months to live. Instead of counting the days Basch recalled the case of the book-keeper in "Grand Hotel," who, having been told that he would die shortly, cast away in his last months all that he had saved during his lifetime. Professor Basch acted similarly. The temperate bachelor who had devoted all his energy to the furthering of medical science, threw himself into the night life. Although he had never tasted champagne, he began to indulge in alcohol. He danced into the night on that thin rope which separated him from death, said his friend at the funeral. This revelry hastened his death, which occurred last week. Professor Basch was a prolific writer on dermatology and venerology. His treatises would form volumes, had he published them in book form. As a teacher at the university he was foremost, as proved by the great number of his pupils."

3. Anti-Rachitic Milk

"Hess states that in endeavors to protect the community from disease our usual concern is to have at our command a specific agent that is effective. In regard to rickets, quite the contrary holds true. An activated milk should be singled out for prophylactic use because it provides a therapeutic measure which is automatic, in that the specific agent is embodied in the food which is essential for the nutrition of the infant and because milk has the distinction and advantage of being the food which contains calcium and phosphorus in the highest degree. Seven years ago the author reported experiments showing that milk can be

activated by means of exposure to ultra-violet energy and a year ago that the milk of cows which are receiving large quantities of irradiated yeast develops high antirachitic potency and may be recommended to protect infants from rickets. Milk can be rendered highly antirachitic by subjecting it for a period of sixteen seconds to the radiations of certain carbon arc rays. In the course of this process it does not develop any disagreeable taste or odor nor is it deprived of its essential vitamins. The department of health in New York established unequivocally that such irradiated milk is able to prevent rickets almost without exception. Biologic assays of this milk showed that it did not vary to a great extent in vitamin D content. It is the established custom to refer to an antirachitic agent such as viosterol, cod liver oil, or irradiated milk as possessing a certain number of antirachitic units per cubic centimeter or per quart. It was found that 35 units of irradiated milk, as determined by the standard rat technic, sufficed to protect a large series of infants. Clinical experiences of this kind are supported by suggestive laboratory observations. Activated milk, in the fluid or dry form, not only possesses the advantage of providing an automatic method of preventing rickets and of supplying this essential factor in a medium rich in phosphorus and calcium but accomplishes this end by means of an exceptionally small amount of the antirachitic factor."

Abstract from Hess, F. A.,  
A.J. of Pub. Health 22:1215  
(Dec) '32; in J.A.M.A. 100:1137,  
(Apr. 8) '33.

#### 4. "Official"

Obviously, if beer contains 3.2 per cent of alcohol having a calory value of 7 per gram, and 10 per cent of nitrogenous and carbohydrate extractive materials having a calory value approximating that of sugars, protein and dextrin, i.e., 4 per gram--and assuming that these "extractive materials" present in beer are utilized in metabolism--a quart of beer will have a value of at least 500 calories. This is five sixths of the calory value of a quart of milk.

One need only ask oneself what the effect of adding 500 calories a day to the diet of a sedentary person already ingesting a ration of liberal food-fuel value would be.

From: Queries and Minor  
Notes, J.A.M.A. 100:1130  
(Apr. 8) '33.

#### VI. MEETING

Date: April 6, 1933

Place: Interne's Lounge, 6th Floor, West Building.

Time: 12:10 to 1:08

Program: Primary Peritonitis

Present: 108

Discussion: Chas. Mead  
Irvine McQuarrie  
N. L. Leven  
L. G. Rigler  
W. P. Ritchie

Theme: C.M.: I am very glad the Editors of this sheet saw fit to let me tell about my son. Anything they would try along this line would be weaker than their usual attempts. My boy - what a subject! I could talk of him for hours without telling you about half his wonderful points. He now weighs about 12 or 21 pounds, eats raw meat, calls for a couple of bottles of 3.2 before breakfast, has a mouthful of teeth, broke his bed the other night when he came in, is already a "mean" shot picking off 2 buffalo, 4 bears, 6 lions, etc. the other evening on his way home from the University. Honestly I feel sorry for the fathers of "ordinary children". My boy is so much smarter than any I have seen yet; well--I see that you cannot understand. What is he going to be? A gentleman, not a surgeon.

I. McQ: Description fits very well our clinical impression. The first case was the only one I have ever seen in which I felt before death the condition was primary peritonitis which

