

THE VALUE OF ASPIRATION LUNG BIOPSY IN DIAGNOSIS

With Illustrative Cases

H. S. VAN ORDSTRAND, M.D. and T. H. LAMBERT, M.D.

Aspiration lung biopsy is a very helpful adjunct in the diagnostic armamentarium of pulmonary disease. It is indicated in roentgenographically visible lesions of the bronchi, parenchyma, and pleura when all other studies (i. e., thorough sputum examinations, bronchoscopy, and bronchography) fail to be of diagnostic aid. With few exceptions, its chief indications follow a negative bronchoscopic examination in cases with nontuberculous lesions, regardless of whether they are of infectious or of neoplastic origin. When indicated, the value of the procedure has proved to well exceed its risk, and when performed with care, it is relatively innocuous.

Some authorities have regarded aspiration lung biopsy as a needless procedure in a peripheral lung tumor when no apparent contraindications to exploratory thoracotomy existed. They reason that the diagnosis as well as further operability of a lesion may be established only on surgical exploration. Our experience has shown that needless exploratory lung surgery has been prevented in certain cases by the use of aspiration needle biopsy, as will be shown in subsequent case reports.

Although aspiration lung biopsy has been performed for more than fifty years, it has been in use with relative frequency only in the past decade. The first diagnostic puncture of the lung was reported by Leyden¹ in 1883. The method was used for the purpose of obtaining organisms from a pneumonic lung. Other early observers mentioned the diagnosis of thoracic cavity tumors by probatory puncture. From 1889 to 1919 fatalities were reported from perforation of intercostal arteries and arteriosclerotic vessels in the lung parenchyma. These were elderly patients in whom rather large trocars were used for thoracenteses. Death was caused by hemorrhage into the pleural cavity, into the lung, and into the bronchi and trachea.

Sixty-five malignant neoplasms proved by needle puncture and aspiration were reported by Martin and Ellis² in 1930. These men were credited with popularizing "aspiration biopsy" and establishing it in the field of neoplastic diseases. In 1936 Sappington and Favorite³ concluded that lung puncture by a needle was a reasonably safe and useful diagnostic procedure. They reviewed more than 2,000 cases of various investigators. Christie,⁴ in 1937, mentioned the value of the examination of cells found in pleural fluid obtained by needle biopsy in a case of pleurisy with effusion complicating the picture of carcinoma of the lung.

Wrenn and Ferder⁵, in describing a new instrument for aspiration biopsy, emphasized the importance of this diagnostic procedure in patients who balk at a cutting diagnostic biopsy. Craver and Binkley⁶ reported 92 cases of suspected primary cancer of the lung in which aspiration biopsies were performed and concluded that the procedure in selected tumors of the lung was a valuable and relatively safe method of diagnosis, and that bronchoscopy will fail as a diagnostic procedure in a substantial percentage of cases of early primary cancer.

Before aspiration biopsy should be considered a means of diagnosis, a thorough history and physical examination should be done, and all systems should be checked carefully for distant primary tumor, although roentgenograms give evidence of a single lesion in the lung. Repeated sputum examinations should be made. If these reports are of no value in establishing a diagnosis, biopsy then may be considered if bronchoscopy is negative, or is not advisable, or is unfavorable.

Tumors may lie below the surface, and an incision through normal tissue might be necessary to obtain a specimen. Aspiration biopsy here may be a time-saving method for securing tissue for histological examination without surgical incision. The danger of dissemination of tissue or fungation of tumor tissue through the operative incision has been theorized by some observers and the surgical risk of obtaining specimens from deep-seated masses sometimes contraindicate surgical biopsy. These are indications for aspiration biopsy.

The incidence of pneumothorax after lung puncture is infrequent, and sudden death is quite rare, the latter in most cases being due to air embolism. If the needle is firmly attached to a syringe, this danger is not very great. Empyema after lung puncture is not increased in our experience. Formerly the procedure was not performed when evidence of a free pleural space was found. Transient hemorrhage has been mentioned by a number of authors. A knowledge of anatomy and physical diagnosis will exclude such accidents as puncture of the heart and large vessels, or an aneurysm.

Sufficient time should be spent in localizing and identifying the exact position of the lesion in the lung field before attempting an aspiration biopsy. Some physicians use roentgenograms placed against the patient's chest while in the sitting position, bony landmarks being correlated with roentgenograms. Identifying marks may be mapped out on the skin and the site of insertion of the aspiration needle marked and visualized firmly in case preparation of the field causes fading of the skin markings.

About one hour before the procedure is begun, the patients are given sufficient sedation to keep them quiet and to allay their apprehension. Mapping out the tumor under fluoroscopic control with the use

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of a boundary of gentian violet painted on the skin prior to the lung biopsy often is helpful. The patient is placed in the sitting position, if possible, and the field is prepared with iodine and alcohol. Prior to the procedure the patient is informed that he may have more cough and may expectorate some blood after the procedure. At the site marked for insertion of the aspirating needle the skin is infiltrated with one per cent novocaine, and the subcutaneous tissues anesthetized in like manner.

The needle and syringe which we use are shown in figure 1. With firm pressure on the stylette, the long 15 gauge needle is inserted into the lung just above a rib margin, care being taken to estimate roughly the thickness and consistency of the pleura while the needle is being inserted. Entrance into the tumor mass can be detected usually by the increased resistance encountered by the needle as compared with the resistance of normal lung tissue. The stylette is withdrawn and the syringe is securely attached to the needle. Suction is created within the syringe by withdrawing the plunger several centimeters and screwing the handle down in position, thus allowing the pressure to remain constant without further manipulation of the plunger. The needle now is withdrawn approximately 2 cm. and is quickly inserted further into the tumor at a different angle with a quick turn to the right, cutting off part of the tumor tissue with the end of the needle, the vacuum retaining the specimen. The needle then is withdrawn from the chest wall, and the suction created in the syringe causes loosened particles of the tumor

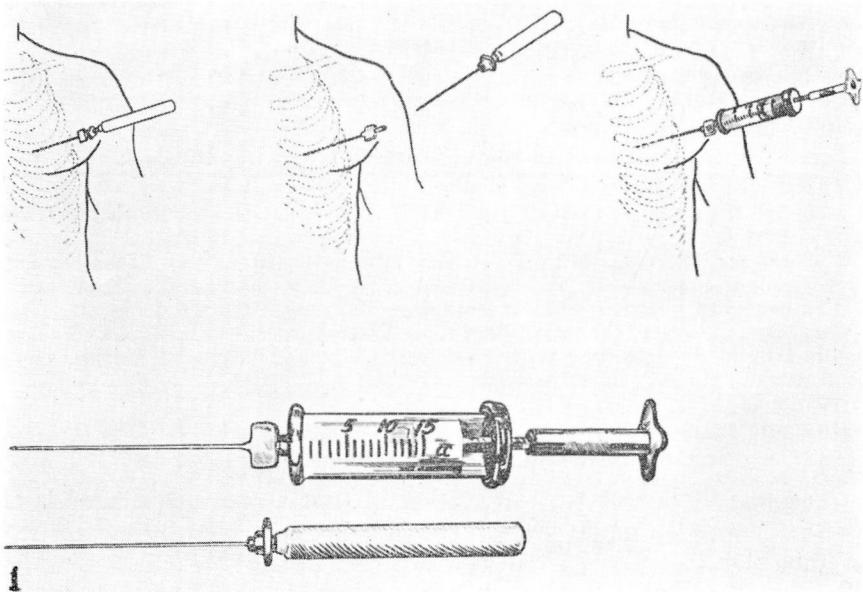


FIGURE 1: Instrument for aspiration biopsy.

tissue to be aspirated into the syringe. If blood enters the syringe during the aspiration, or if the patient starts to cough, the needle should be withdrawn immediately.

The aspirated material is sent to the pathological laboratory and a part to the bacteriological department (when indicated) where the precipitate is sectioned for microscopic study. It is fixed in formaldehyde and is then centrifuged. If the amount of aspirated material is small, it is centrifuged and the precipitate fixed with absolute alcohol for sectioning and study.

Aspiration biopsy has been used to a distinct advantage in establishing a diagnosis of pulmonary lesions in certain cases at the Cleveland Clinic when all other methods had been of no value.

The following cases of pulmonary lesions have been selected for presentation because of certain interesting features. They are of clinical interest because the impression prior to the biopsy procedure in most instances was at wide variance with the microscopic findings.

Case 1: R. H. S., a 49 year old man, was seen on February 5, 1940, complaining of low-grade fever and tachycardia of two months' duration. There had been a dull pain anteriorly in the upper left chest for one month. He had lost 12 pounds in weight during the two months' time.

A presumptive diagnosis of aneurysm had been made elsewhere. The entrance films are shown in figure 2A in which a mass is delineated in the upper left lung adjacent to the mediastinum.

The general physical examination was not contributory other than the presence of a dullness anteriorly between the levels of the first and third ribs on the left side, with an occasional moderate to coarse crepitant râle in this area. There were no objective signs of cardiovascular disease. The temperature was 99.2°F.

Bronchoscopic examination revealed considerable fixation of the trachea in the region of the mass, but no evidence of tracheobronchial ulceration. Fluoroscopy revealed no pulsation of the mass.

Under fluoroscopic control an aspiration needle biopsy was obtained. There was microscopic evidence of carcinoma (Fig. 2B).

Although the lesion was felt to be clinically inoperable, exploratory thoracotomy was performed at the insistence of the family. The tumor mass was found to involve the upper lobe of the left lung, and to extend well out into the superior mediastinum. The mass was quite firm and about the size of an orange. It was immobile and firmly attached to all surrounding tissues so that excision was impossible. The final diagnosis was bronchogenic carcinoma of the medullary type. The tumor cells were of fairly uniform structure with no tendency to form glands or pearls. Mitotic figures were numerous and in some areas the tumor cells were columnar in type and apparently secreted mucus.

The postoperative convalescence was uneventful. A course of roentgen therapy was administered to the lung tumor. Two subsequent courses were given in the ensuing ten months. The patient died of his disease one year after first being seen here.

Comments: This case was interesting in that a previous diagnosis of aneurysm had been made, this diagnosis being corrected by the aspiration lung biopsy.

Case 2: A. P., a 55 year old man, was first seen on January 27, 1940, with the chief complaint of soreness in the right chest. There had been a gradual development of

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tenderness in the right upper chest for a year, and a tight feeling substernally. He developed a chronic cough which became more pronounced two weeks prior to his visit here. The sputum was blood-tinged. He had lost 15 pounds of weight in a year. A previous impression of his illness had been tuberculosis.

Physical examination revealed decreased expansion of the right lung, diminished tactile and vocal fremitus in the right upper chest from the apex down to the level of the seventh interspace anteriorly and the seventh thoracic vertebra posteriorly, with dullness to percussion over this area. There was a definite expiratory rhonchus over the entire right chest and numerous coarse and crepitant râles were heard in the right lateral upper lung field.

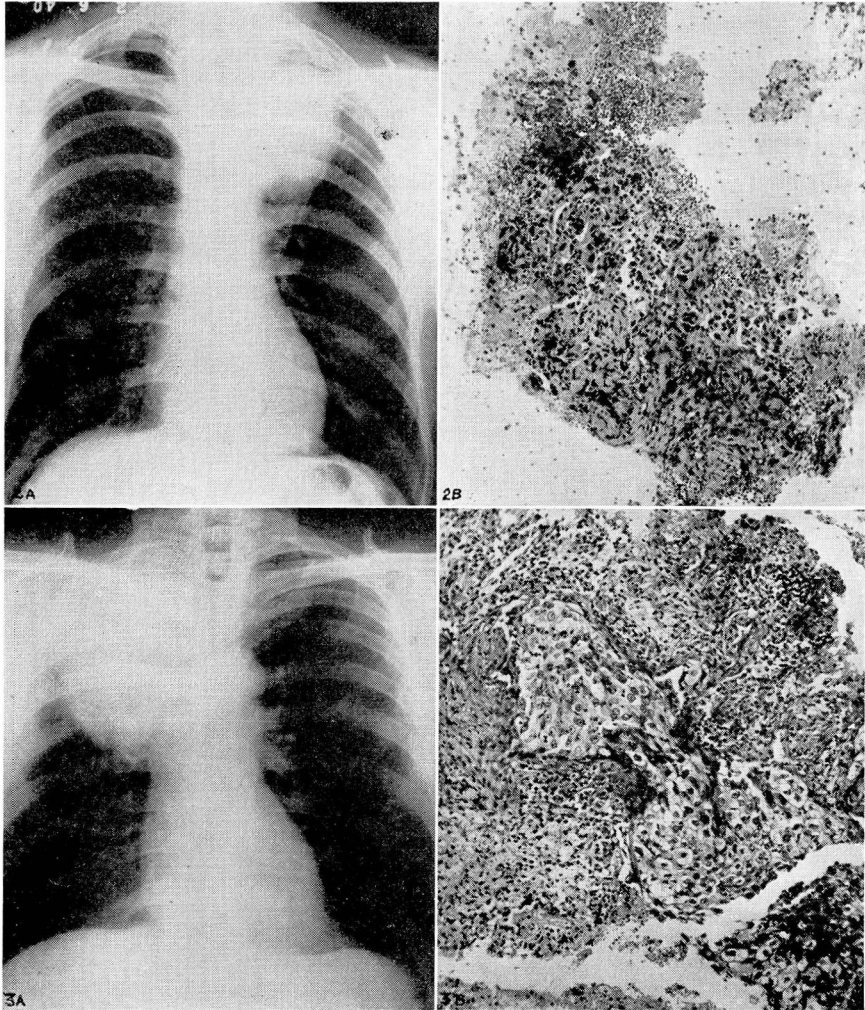


FIGURE 2: A. Bronchogenic carcinoma, upper left lung.

B. Photomicrograph showing medullary type of bronchogenic carcinoma.

FIGURE 3: A. Bronchogenic carcinoma, upper right lung.

B. Aspiration biopsy of lesion.

Roentgen examination of the chest showed a marked mottled density in the right upper lung extending down to the level of the lower border of the third anterior rib (Fig. 3A).

Bronchoscopic examination revealed the tracheobronchial tree to be entirely clear as far as could be determined.

In the aspiration needle biopsy the needle was inserted in the right first interspace, one and one-half inches from the sternal border. The microscopic examination of the sections showed fragments of tissue which appeared to be a bronchial mucosal type without tumor, along with numerous small and fairly large fragments of tumor tissue consisting of masses of large epithelial cells not forming glands or pearls (Fig. 3B).

On February 24, 1940 a right pneumonectomy was done. The patient died of empyema on the fourth postoperative day. The diagnosis was bronchogenic carcinoma.

Comment: In this patient a tentative diagnosis of tuberculosis was found to be incorrect on aspiration biopsy, carcinoma being found.

Case 3: G. R. O., a 75 year old man, presented himself for examination on November 22, 1940 with symptoms of a chronic productive cough, weakness, and night sweats of three months' duration.

The general physical examination revealed a temperature of 100.4°F. with positive findings in the right lung which consisted of a decreased note posteriorly from the levels of the second to the fifth thoracic vertebrae.

Roentgen examination of the chest revealed a well circumscribed ovoid shadow in the upper right lung (Fig. 4A, right lateral view). This was interpreted as probably being due to an interlobar empyema.

A bronchoscopic examination was negative.

Aspiration lung biopsy revealed the presence of tumor cells. No fluid was obtained. The photomicrograph of the biopsy is shown in figure 4B.

A clinical diagnosis of bronchogenic carcinoma was made.

The patient had subsequently received courses of roentgen therapy with slight improvement.

Comment: In this case a clinical impression had been made of interlobar empyema and the aspiration lung biopsy proved the lesion to be a solid lung tumor.

Case 4: C. W. W., a 63 year old woman, entered the Clinic with a history of a palpable goiter of twenty-five years' duration, symptoms of intermittent hyperthyroidism of ten to twelve years' duration, and a chronic nonproductive cough of two months' duration.

The general physical examination revealed an enlarged modular goiter, with abnormal signs in the right chest. There was dullness over the right lung posteriorly in the level of the eighth to tenth vertebral spine, with decreased to absent breath sounds over this region and a few fine moist râles.

Roentgen examination (Fig. 5A) revealed evidence of a thickened pleura between the right middle and right lower lobes with some degree of effusion. No tumor mass was delineated. The fasting blood cholesterol was 171 mg. per cent, and the basal metabolic rate was plus 18 per cent.

On bronchoscopic examination no direct evidence of tumor was found, although the mediastinum was noticeably greatly thickened and the floor of the right main stem bronchus was pushed upward, as if by a mediastinal mass. No intrinsic lesion was noted.

Aspiration lung biopsy showed masses of tumor cells of variable size with many mitotic figures and atypical nuclear division (Fig. 5B). It had the appearance of carcinoma, and a clinical diagnosis of bronchogenic carcinoma was made.

The patient was advised to have roentgen therapy, which was carried out elsewhere.

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Comment: In this patient, no tumor mass was delineated on the roentgenogram, the latter giving a picture of an interlobar effusion. The bronchoscopic examination gave indirect evidence of tumor, the diagnosis being confirmed by aspiration lung biopsy.

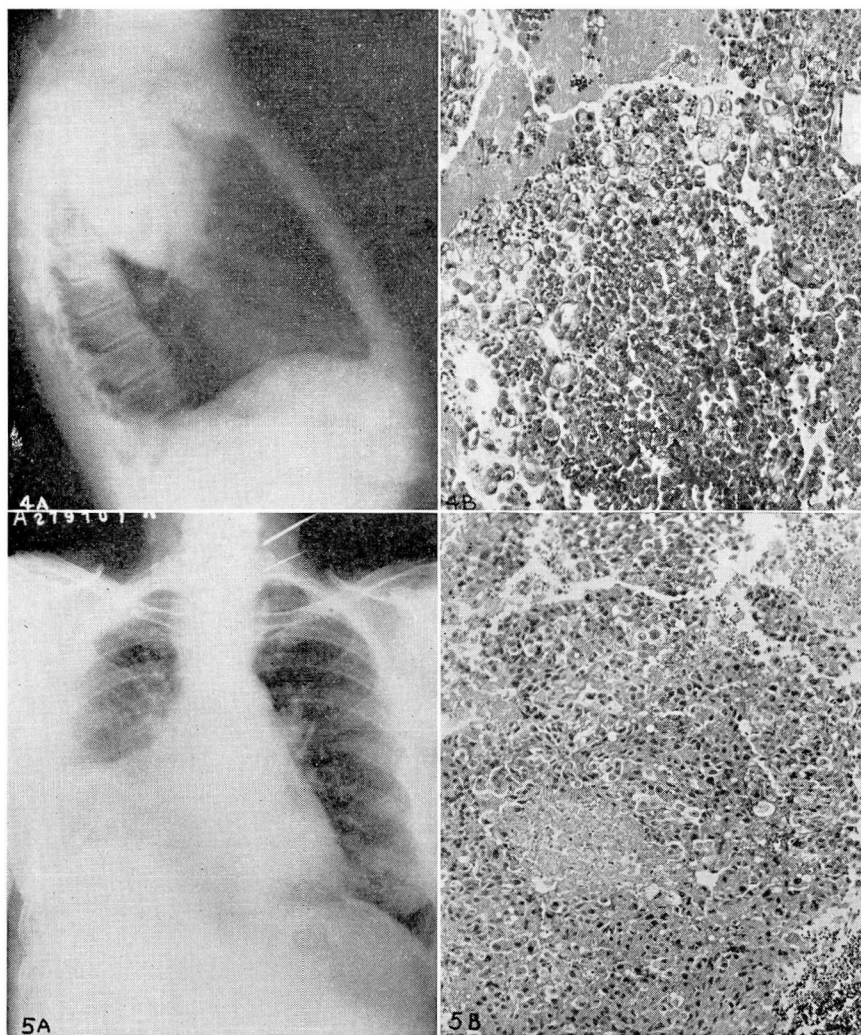


FIGURE 4: A. Lesion suggestive of interlobar empyema as seen in right lateral roentgenogram.

B. Aspiration biopsy revealed solid tumor of bronchogenic type.

FIGURE 5: A. Right lower lobe lesion simulating interlobar effusion with no visible tumor mass.

B. Photomicrograph of aspirated material showing tumor cells of bronchogenic type.

Case 5: P. S., a 21 year old college student was seen on May 18, 1940, with symptoms of a dull pain in the lower right chest anteriorly of five months' duration, and fever and shortness of breath of two weeks' duration. A roentgenogram taken two months previously (Fig. 6A) revealed a fairly circumscribed shadow the size of a grapefruit in the lower right lung. The admission film (Fig. 6B) revealed a massive effusion on the right and the physical signs were entirely those of a total right pleural effusion. The patient's temperature on admission was 101.0°F., and he was quite dyspneic.

On three successive days a total of 5600 cc. of bloody fluid were withdrawn from the right lung by aspiration. Microscopical studies revealed tumor cells (Fig. 6C). The tumor cells were of a highly undifferentiated sarcomatous type suggestive of sympatheticoblastoma. A subsequent surgical biopsy through the anterior chest wall revealed identical cellular structure.

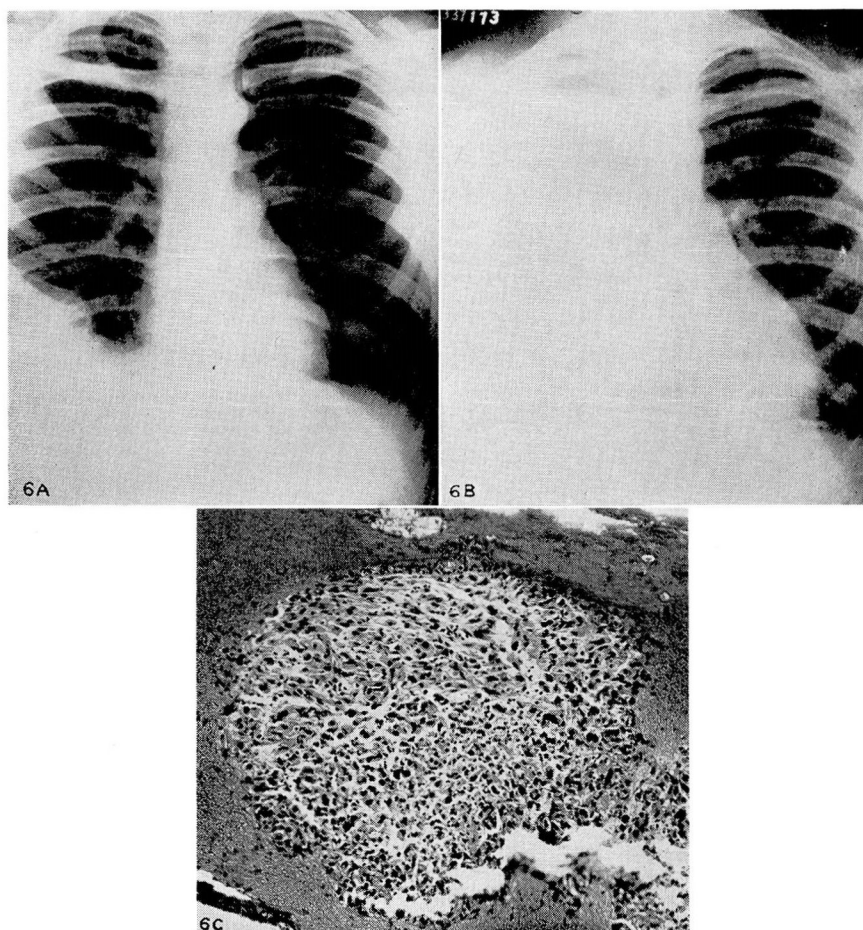


FIGURE 6: A. Circumscribed lesion seen in lower right chest on films made elsewhere previously.

B. Total right pleural effusion on admission.

C. Tumor cells in bloody pleural fluid (at aspiration biopsy). Microscopically, sympatheticoblastoma.

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Under intensive irradiation therapy the patient improved markedly for a time with complete disappearance of the tumor. However, he died nine months later from widespread multiple metastases.

Comment: In this patient the diagnosis was confirmed by the identification of the tumor cells in aspirated pleural fluid.

Case 6: A. B. B., a 46 year old man, was seen on July 16, 1940 referable to pain in the left scapular area radiating to the left arm, of four months' duration.

Physical examination revealed a decreased note over the upper third of the left chest posteriorly, associated with bronchial breathing and increased vocal and tactile

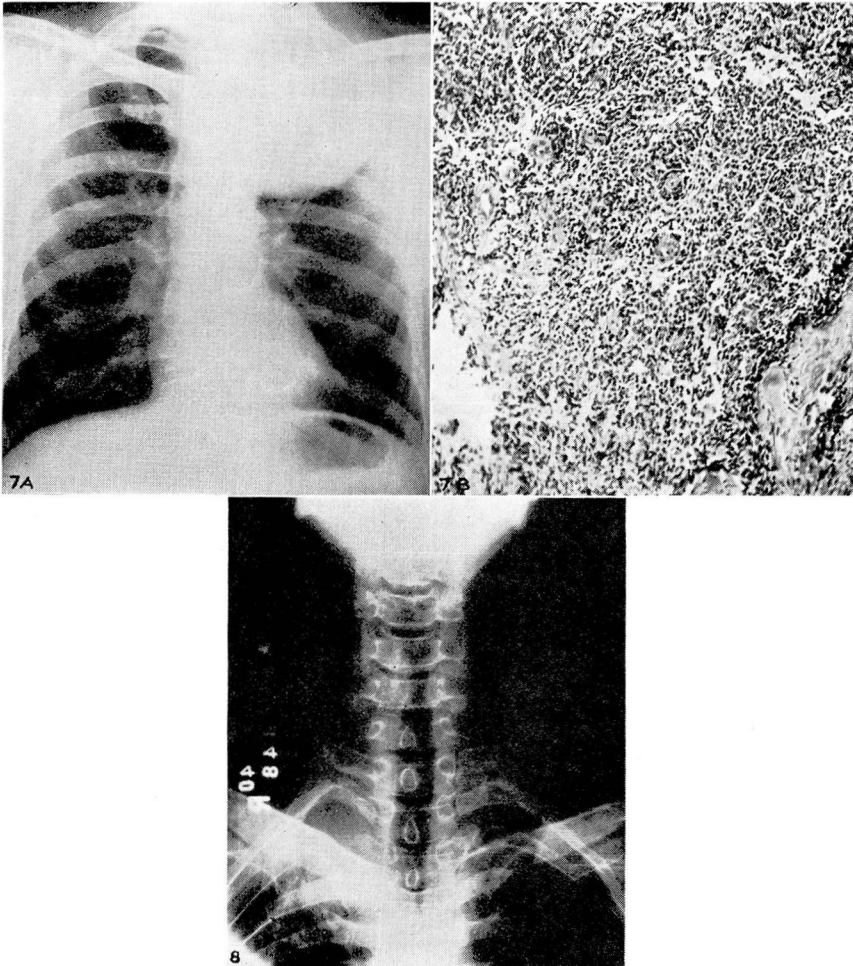


FIGURE 7: A. Circumscribed lesion, upper left lung.

B. Photomicrograph of aspirated material revealing bronchogenic carcinoma.

FIGURE 8: Right superior sulcus tumor with partial destruction of posterior portion of third rib. Aspiration biopsy revealed carcinoma of bronchogenic type.

fremitus. There were a few inspiratory moist râles in the upper left chest anteriorly and in the upper left axilla. A definite left Horner's syndrome was noted. The roentgenogram (Fig. 7A) was interpreted as showing a probable superior sulcus tumor.

Bronchoscopic examination was negative.

The aspiration lung biopsy revealed the presence of carcinoma, as noted in the photomicrograph (Fig. 7B).

In spite of intensive irradiation, he steadily became worse and died one month later. At necropsy, primary carcinoma of the left lung with infiltration of the pleura and thoracic vertebrae, and metastases to the mediastinal nodes and right adrenal were found.

Comment: In this patient the histological appearance of the tumor was demonstrated by aspiration lung biopsy. The lesion was clinically inoperable, as indicated by the presence of the Horner's syndrome.

Case 7: R. L., a 50 year old man, entered the Clinic on December 28, 1940 with symptoms of pain in the right scapular region, radiating down the inner aspect of the right arm, of two months' duration.

The physical examination revealed no significant findings other than the presence of a right Horner's syndrome.

The roentgen examination (Fig. 8) revealed a shadow in the extreme right apex with partial destruction of third posterior rib. The diagnosis was a probable superior sulcus tumor.

Aspiration lung biopsy revealed a definite carcinoma, and a diagnosis of bronchogenic carcinoma of the superior sulcus type was made.

The patient has received palliation to date with no change in the size of the tumor mass on intensive irradiation therapy.

Comment: This patient illustrates the aid of aspiration lung biopsy in microscopic confirmation of an inoperable superior sulcus tumor.

In the two following cases, a diagnosis of metastatic lesions was obtained through aspiration biopsy.

Case 8: E. N., a 52 year old woman, was seen on March 15, 1940 complaining of "chest heaviness" and shortness of breath of three months' duration. A left pleural effusion had been recognized two months previously subsequent to which time six thoracenteses were done with negative findings referable to tuberculosis.

The physical signs were those of a bilateral pleural effusion (Fig. 9A). There was no identifiable parenchymal lesion because of the extensive effusion.

Bronchoscopy revealed negative findings. The aspiration of pleural fluid revealed the presence of probable metastatic malignant cells (Fig. 9B).

The patient died of her disease a few weeks later. At necropsy papillary adenocarcinoma of the left ovary was found with widespread pleural metastases.

Comment: In this case aspiration study was of value in that tumor cells were found in pleural fluid which were identified as not being of primary lung origin.

Case 9: F. E. G., a 56 year old woman, was seen on August 2, 1939 with the chief complaint of recurrent attacks of pain in the upper right quadrant. As a minor symptom she mentioned a dull pain in the upper left chest anteriorly with "soreness in the left side of her neck" of six weeks' duration. The past history was negative. A left mastectomy had been done six years previously, at which time a diagnosis of carcinoma had been made.

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The general physical examination was negative, other than the presence of moderate tenderness in the region of the gall bladder. Roentgen examination of the chest revealed a well circumscribed mass in the upper left chest (Fig. 10A). Cholecystography showed a poorly functioning gallbladder with cholelithiasis. Clinical diagnoses of chronic cholecystitis with cholelithiasis and of probably dermoid cyst of the upper left mediastinum were made.

An aspiration lung biopsy was done in the left upper lung field at the second inter-space at the level of the junction of the middle and inner third of the clavicle. Thick,

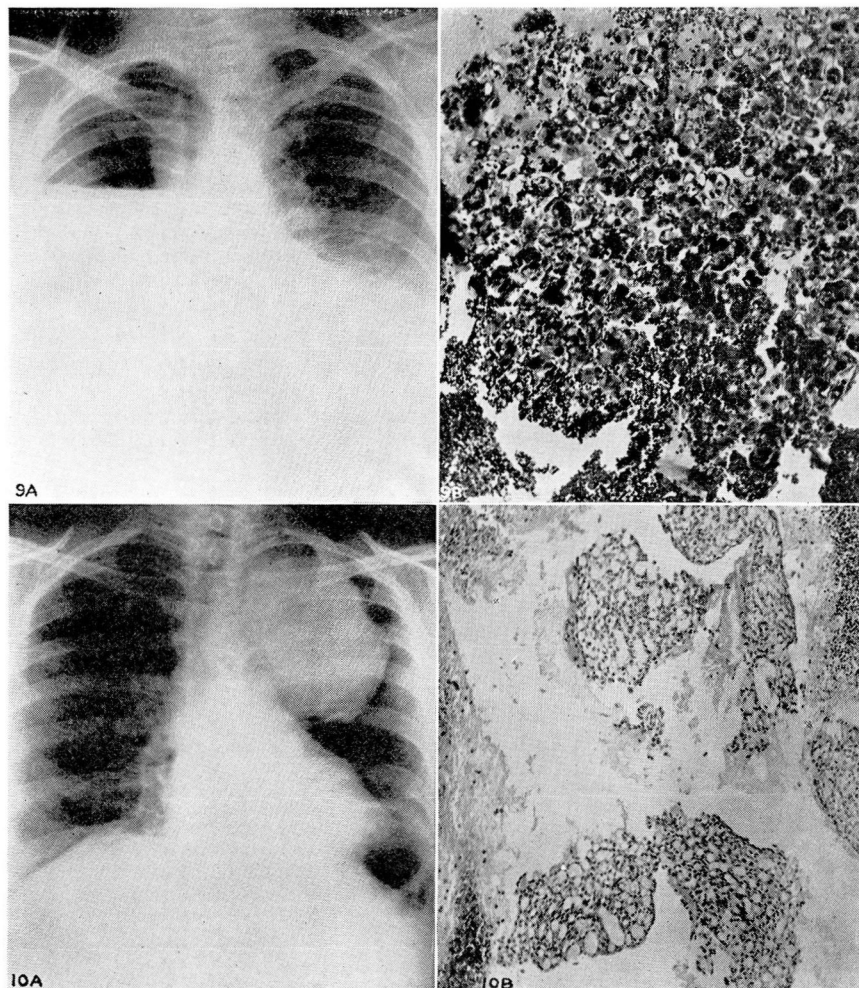


FIGURE 9: A. Bilateral pleural effusion.

B. Aspiration biopsy revealed the pleural fluid to contain metastatic cells. Pleural metastases from papillary adenocarcinoma of left ovary were later found at necropsy

FIGURE 10: A. Solitary circumscribed lesion, left upper lung. Clinical impression; primary carcinoma or dermoid.

B. Aspiration biopsy revealed coil gland carcinoma (identical to slide obtained of breast tumor removed six years previously).

bloody, yellowish-white material was obtained. Microscopic examination (Fig. 10B) revealed masses of small, deeply staining epithelial cells showing some tendency to form tubular or gland-like structures and to form cylindromatous modules. The tumor had the histological characteristics of a coil-gland carcinoma of the breast. On obtaining the slide of the original breast tumor from another hospital, the microscopic appearance was found to be identical.

The patient obtained some palliative improvement on intensive irradiation therapy but died from the metastatic lung lesion six months later.

Comment: In this case a solitary lung tumor on aspiration lung biopsy was found to be a metastatic coil-gland carcinoma and needless lung surgery was prevented.

The two following cases illustrate the aid of aspiration lung biopsy in the diagnosis of inflammatory lesions.

Case 10: R. K., a 46 year old man, was seen on July 20, 1939 with the chief complaint of a persistent cough. He had had lobar pneumonia three months prior to admission, followed by a dry cough, the previous four weeks being associated with profuse mucopurulent sputum and bouts of fever. There was a loss of 50 pounds in weight since the pneumonia. A partial exploratory thoracotomy had been performed elsewhere one month prior to being seen at the Clinic, at which time a presumptive diagnosis of lung tumor had been made.

Upon physical examination the patient was found to be decidedly malnourished. There was limited expansion in the right chest with a dull to flat percussion note on this side posteriorly from the level of the fifth to the ninth thoracic vertebra. Breath sounds were absent in this area and a few crepitant râles were heard in the right midaxillary region.

Roentgen examination of the chest (Fig. 11A) revealed a haziness of the lower half of the right lung which was interpreted as being due to thickened pleura along with parenchymal infiltration. There was no identifiable tumor mass roentgenologically.

Upon bronchoscopic examination no pathology was observed.

Aspiration lung biopsy revealed no tumor tissue. A Type III pneumococcus was found both in the smear and on typing, and a tentative diagnosis of so-called unresolved pneumonia was made.

The patient was sent home for a course of sulfanilamide therapy. He obtained prompt relief of his symptoms and when seen eight months later, the lung was entirely normal clinically and roentgenologically (Fig. 11B).

Comment: In this patient the finding of a type-specific pneumococcus along with negative biopsy for tumor tended to rule out a previous impression of neoplasm and the subsequent course verified the diagnosis of an inflammatory lesion.

Case 11: O. D., a 46 year old colored woman, came to the Clinic on November 1, 1939 with symptoms of the insidious onset of a chronic cough, fever, and dull pain in the anterior left chest, of two months' duration. A previous diagnosis of lung tumor had been made by roentgen examination.

Physical examination revealed decreased percussion notes in the left midlung field over an area of two ribs in width, with a few associated fine crepitant râles. The patient was noted to have a so-called blue-gummed appearance with considerable gingivitis.

Roentgen examination (Fig. 12A) showed a dense, fairly well circumscribed shadow the size of an orange in the anterior axillary line of the left midlung field. No cavity was seen. Repeated sputum examinations were negative for acid-fast organisms and

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other pathogens, except for an unusually large number of fusiform and spirochetal types.

Bronchoscopic examination was entirely negative. The left main stem bronchus with its divisions was well visualized and there was no evidence of tumor, nor purulent material.

The aspiration biopsy approach was made anteriorly just midway between the hylum and the peripheral lung zone, no resistance being found on entering the mass, and a large quantity of very foul pus was aspirated. Microscopic examination of the aspirated

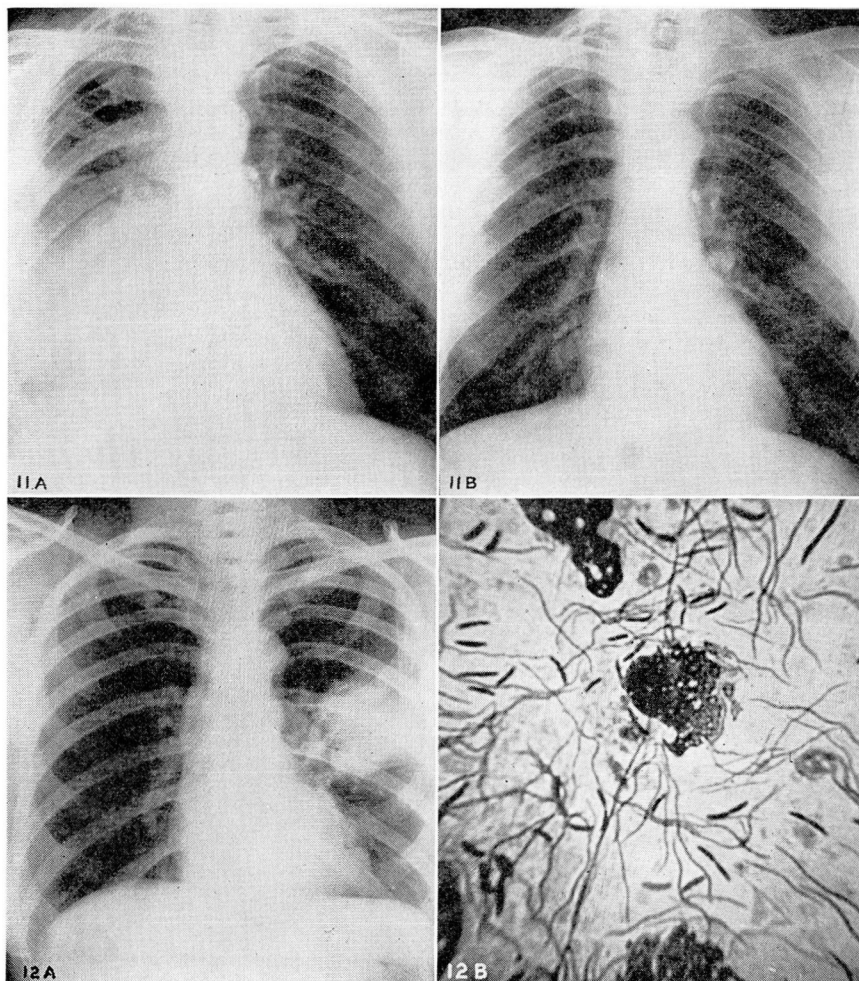


FIGURE 11: A. Lesion, right lower lung. History and previous studies suggestive of bronchogenic carcinoma.

B. Aspiration biopsy negative for tumor cells. Type III pneumococcus isolated. Roentgenogram following chemotherapy.

FIGURE 12: A. Lesion, left lung, referred with clinical impression of tumor.

B. Aspiration revealed typical fusospirochetal lung abscess. Smear of aspirated material reveals fusiform and spirochetal elements of Vincent's group.

material (Fig. 12B) revealed numerous fusiform and spirochetal organisms of the Vincent's type both on the smear and under darkfield examination. A diagnosis of a fusospirochetal lung abscess was made. Surgery was advised but the patient refused this. Marked improvement on medical management occurred in the ten days before leaving the hospital. However, the patient later developed pneumonia and expired.

Comment: In this patient aspiration lung biopsy established a diagnosis of a fusospirochetal lung abscess where a previous tentative diagnosis of lung tumor had been made.

Case 12: D. S., a 51 year old man was referred to the Clinic on May 26, 1941 with the symptoms of cough, dysphagia and weight loss (20 pounds) of four months' duration.

The physical examination revealed a decreased note in the upper right lung adjacent to the mediastinum. The roentgen examination of the chest outlined a fairly

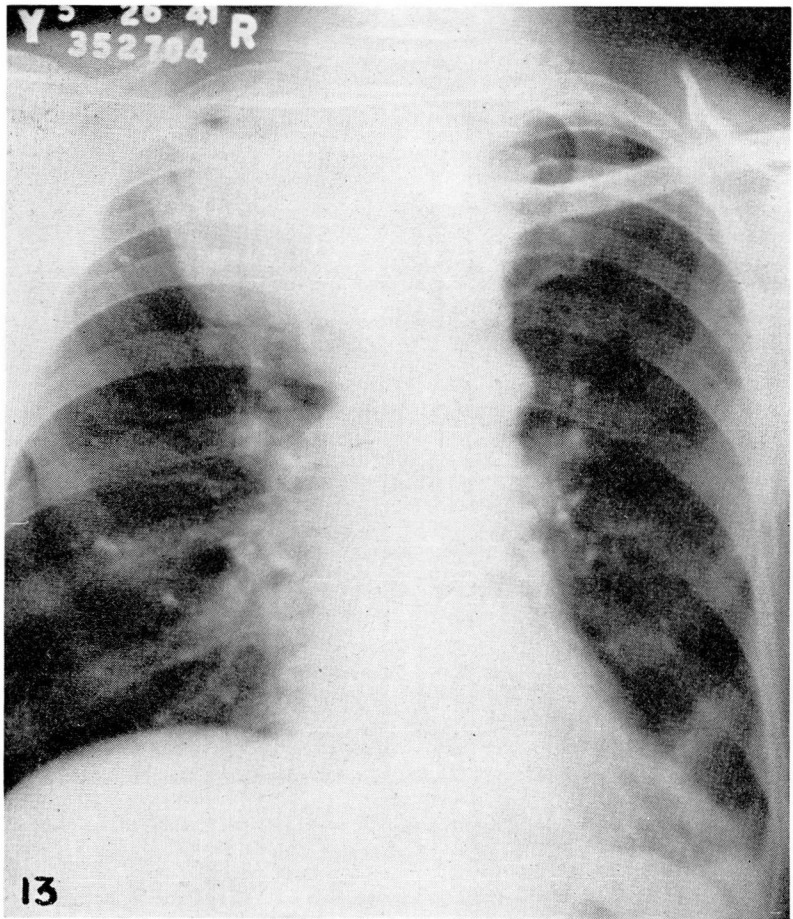


FIGURE 13: Lesion of right upper lung. Aspiration biopsy revealed squamous cell bronchogenic carcinoma.

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smooth mass in the upper right lung adjacent to the mediastinum as seen in figure 13. An esophogram was normal except for displacement to the left and anterior by the extrinsic lesion.

Bronchoscopy showed some degree of tracheal fixation but did not visualize the lesion.

Aspiration biopsy was made, the needle being inserted in the right second posterior interspace and the diagnosis of squamous cell bronchogenic carcinoma established microscopically. The lesion was concluded to be inoperable clinically because of the tracheal fixation, and roentgen therapy was advised.

Comment: This patient illustrates the frequent upper lobe primary lung tumor where tissue for biopsy is often unobtainable bronchoscopically (this being due to mechanical difficulty in seeing beyond the upper lobe orifice with the instrument).

SUMMARY

Aspiration biopsy is often a very helpful diagnostic procedure in patients exhibiting roentgenologic disease of the bronchopulmonary tract or pleura where other measures fail. It is of value in certain inflammatory lesions, as well as in primary or metastatic neoplasms.

When done with care, aspiration biopsy is a simple and relatively safe procedure. When indicated, its value exceeds its risk. The technic, with the instrument used, is described and a series of 12 illustrative cases are presented.

REFERENCES

1. Leyden, Cited by Craver and Binkley: Aspiration biopsy of lung tumors, *Thoracic Surg.* 8:436-463 (April) 1939.
2. Martin, H. E. and Ellis, E. B.: Biopsy by needle puncture and aspiration, *Ann. Surg.* 92:169-181 (August) 1930.
3. Sappington, S. W. and Favorite, G. O.: Lung puncture in lobar pneumonia, *Am. J. M. Soc.* 191:225-234 (February) 1936.
4. Christie, A. C.: Diagnosis and treatment of primary cancer of lung (Silvanus Thompson memorial lecture) *Brit. J. Radiol.* 10:141-158 (March) 1937.
5. Wrenn, F. and Ferder, J. M.: New instrument for aspiration biopsy, technical procedure combining principles of tissue punch and improved aspiration syringe, *South. M. J.* 32:320-322 (March) 1939.
6. Craver, L. F. and Binkley, J. S.: Aspiration biopsy of tumors of lung, *J. Thoracic Surg.* 8:436-463 (April) 1939.