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Contributors

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Royal College of Surgeons of England

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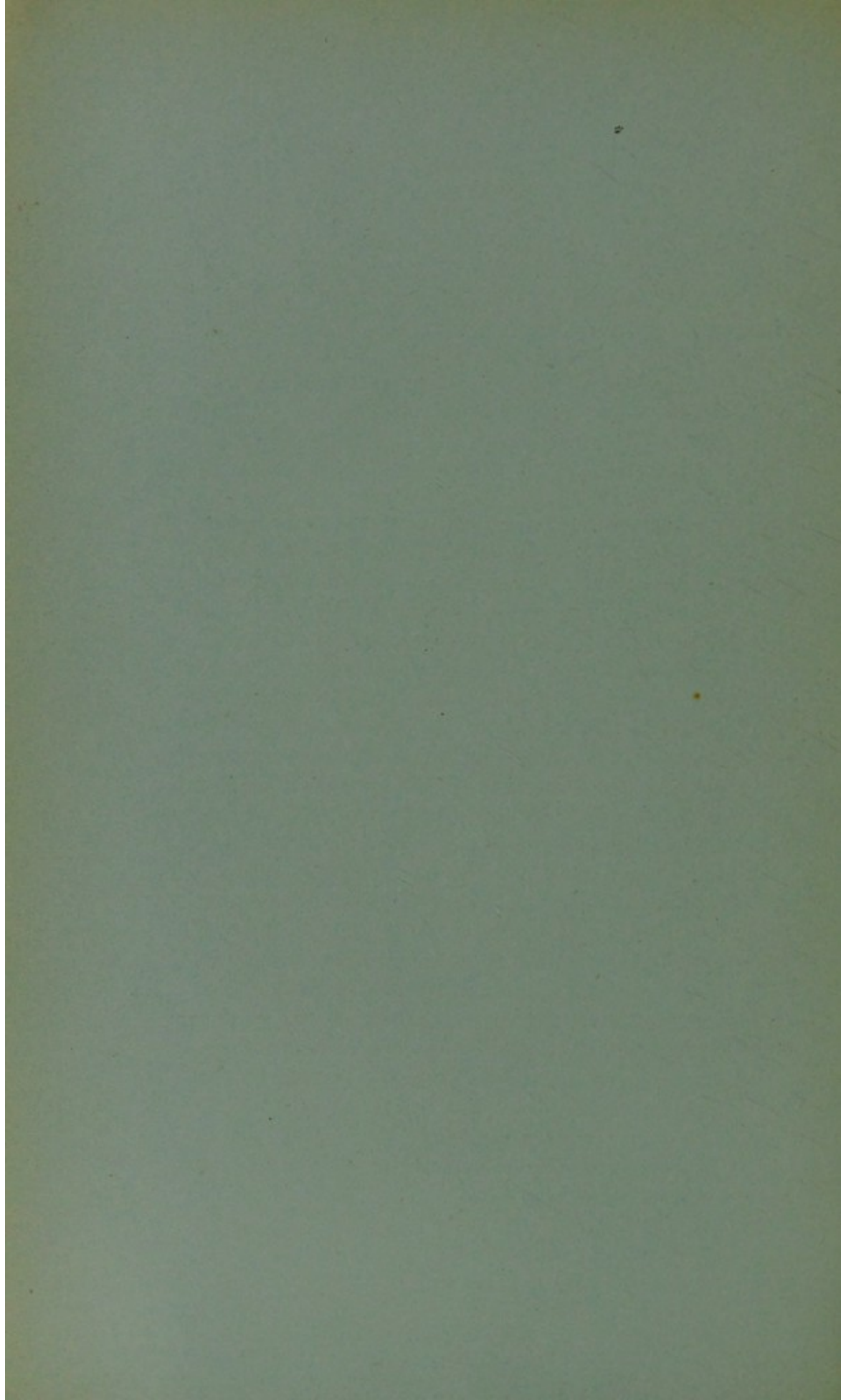
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BY
J. H. MUSSER, M.D.



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PRIMARY CANCER OF THE LUNG.

BY J. H. MUSSER, M.D.,
*Professor of Clinical Medicine, University of
Pennsylvania.*

DURING the past eighteen months three cases of cancer of the lung have come under the observation of the writer. The diagnosis of two was verified by autopsy; the clinical course of the third seems to be conclusive. The first case was one of massive tumor of the lower lobe of the right lung, with a few scattered nodules in the other lobe, and metastases in the liver and the lymph nodes of the thorax. It is referred to in the article on cancer of the lung, fourth volume of the system of medicine of Nothnagel. No further reference will be made to it in this paper except to repeat that the clinical course and physical signs were those of a pleuropneumonic infection. Pain was the first symptom, but it soon disappeared. Signs of effusion were present, but aspiration and exploration were negative, the latter revealing the nodule in the lung. Fever of moderate degree, 101° F. at the highest, with well-marked leucocytosis, was present throughout the disease. Cachexia did not appear until very late. The liver involvement was shown by a large, non-fluctuating mass, which grew rapidly. The duration was less than three months. The

patient was a male, aged forty-nine years, in whose family, social, or previous medical history there was nothing suggestive.

The second case will be the subject of this report. The third was a male, aged seventy-one years, who had a cough for six months; loss of flesh and strength; a very large pleural effusion of three weeks' duration, which, when aspirated twice, did not lessen an area of dulness in the left axillary and post-thoracic region. The fluid was very bloody, but did not show any cellular elements suggestive of carcinoma. Aspiration was performed twice. Prostration and emaciation continued. The supra-clavicular and cervical lymph nodes on the left side enlarged and became indurated, seeming like secondary metastases. Removal for examination was not permitted. Death took place from asthenia at the end of nine months from the appearance of the effusion. The involvement of the lymph nodes seemed to prove the nature of the process to be carcinoma.

The case which is the subject of this report was of special interest because of its rapid course, its unusual onset, its resemblance, clinically, to tuberculous bronchopneumonia, and the resemblance of the lesions, macroscopically, to that process. Indeed, until sections were made it appeared to the naked eye to be a diffused, caseous pneumonia of tuberculous origin.

CASE.—H. B., aged forty-seven years, clerk, single; residence, Pennsylvania; consulted me December 12, 1902. Not closely confined and duties not arduous; no exposure; habits regular. Eats hurriedly; smokes moderately; no alcohol; moderate tea and coffee.

Always healthy ; no syphilis. At fifteen years had injury to bone, the effects of which entirely disappeared. Had a very severe attack of influenza in 1890 ; dysentery in 1902. Weight ten years ago, 165 pounds. Family history excellent.

Present Condition. Complains of indigestion, sore throat at night, expectoration of mucus, dyspnœa on exertion, loss of flesh, and weakness. The gastric symptoms and sore throat continued since the attack of dysentery in August. The expectoration has been increasing for four months. The loss of flesh has been noted for three months.

The special characteristics of the symptoms must be noted. The sore throat was present at night, and even then only in the recumbent posture. In the day, if he would lie down, it would return, to be relieved immediately on rising. The expectoration was remarkable. A moderate cough would be attended by the welling up of large amounts of fluid, so that when I saw him spitting was one of the most distressing symptoms. Indeed, cough did not by any means bring up the fluid ; it simply welled up from the pharynx and œsophagus. The patient estimated that three pints were discharged. Headache was more or less constant, but only when the patient was stooping. Dyspnœa has been progressively increasing the past month. Sleeplessness has been a very distressing symptom.

Physical Examination. Fairly well nourished ; sickly appearance ; anxious expression ; voice clear, but weak ; skin normal ; no eruptions, no œdema ; tissues flabby ; weight, 140 pounds ; temperature normal ; slight enlargement of right lobe of thyroid gland ; eyes normal.

Heart normal size ; sounds normal ; action rapid ;

pulse 100 to 110, 120 to 130 on exertion; respiration, 28 to 32; no difference of two sides. No signs in lungs except a slight pleural friction in right axillary region. Resonance skodaic over right base. Nothing unusual on abdominal examination. Stomach-tube of good calibre passed without difficulty.

Laboratory Examinations. Sputum clear, mucoid, and slightly purulent; microscopically some pus; no tubercle bacilli; diplococci in moderate numbers. A second specimen same results, except some blood.

Blood. Hæmoglobin, 80 per cent.; red blood corpuscles, 4,000,000; white blood corpuscles, 12,000.

Gastric Contents. After test meal 30 c.c., some mucus, small amount of bread. Total acidity, 30; free HCl.

Urine. 1020; no albumin or sugar. Microscopic examination negative.

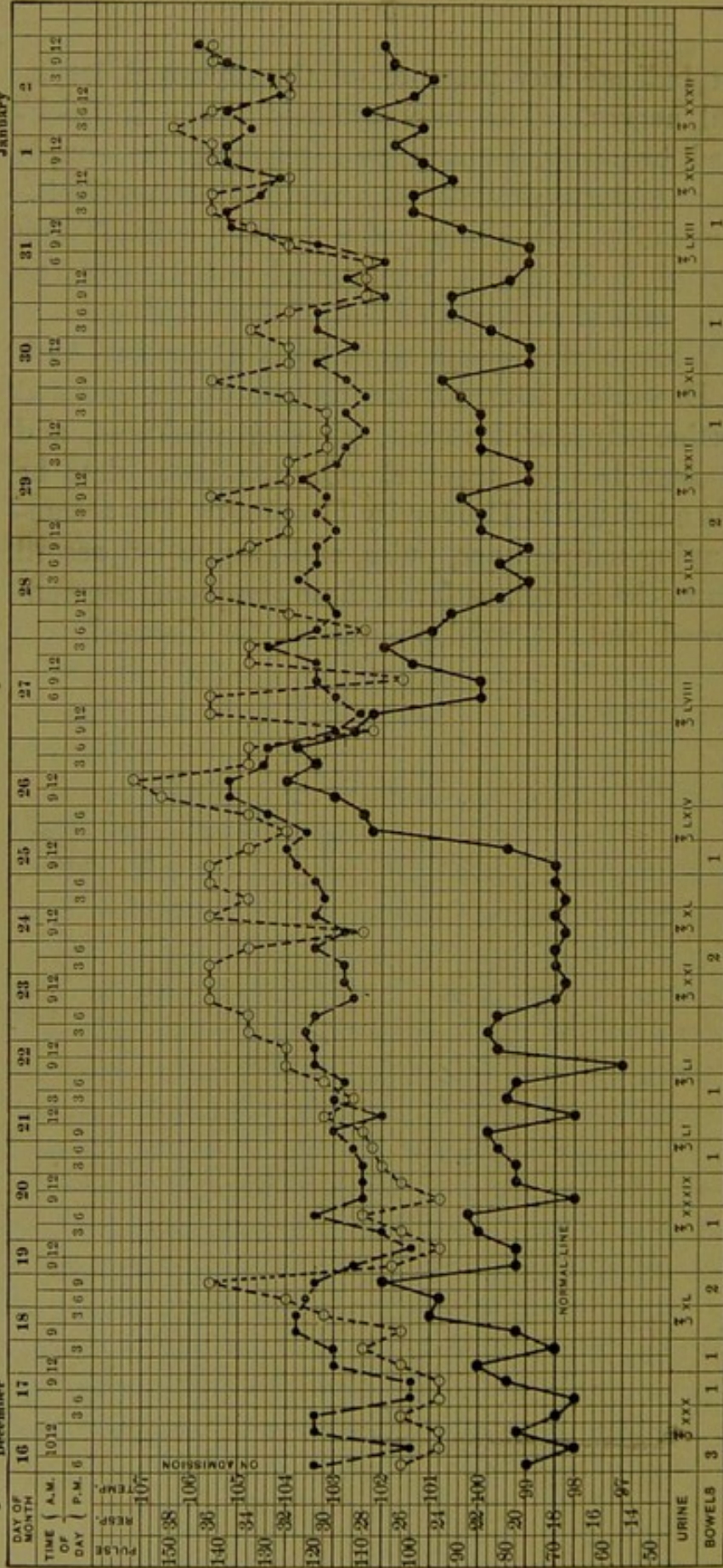
Nose, Fauces, Larynx. Dr. Bliss says: "There is no infiltration of the larynx suggestive of tuberculosis or syphilis. The entrance to the œsophagus, as nearly as it can be seen, appears normal. There is no bulging forward of the posterior wall of the larynx or trachea suggestive of a new-growth in the œsophageal wall. The lymphoid tissue at base of tongue is not in abnormal excess. The entire mucous membrane of the nose, nasopharynx, pharynx, and larynx shows considerable catarrhal inflammation, as indicated by proliferation and desquamation of the superficial epithelium and an excessive flow of thick, tenacious mucus, considerable quantities of which come from the nose and nasopharynx. The action of the vocal cords does

not indicate any pressure on the recurrent laryngeal nerves. The interarytenoid space is thickened, but only, I think, as a result of the simple pharyngolaryngitis, not as a result of a specific inflammation or beginning of a new-growth. There seemed to be a very pronounced pulsation of the right carotid in excess of that of the left side."

While under observation from December 12th to December 16th, patient became worse, alarmed particularly about throat, growing weakness, and absolute loss of appetite. On the latter date he was admitted to University Hospital. The accompanying temperature, pulse, and respiration record shows the course, as far as these symptoms are concerned, and the rapid progress of the disease :

December

January



PULSE ——— RESP. - - - - - TEMP. ———

December 16, 1902. Physical examination by Dr. Sailer. There is slight prominence of the precordium; sternum is slightly funnel-shaped; the intercostal spaces distinct; pulse small, rhythmic. Apex-beat is weak, circumscribed, fifth interspace in nipple line. No diastolic shock; no cardiac impulse. Area of cardiac dulness diminished. Heart sounds are clear, but faint; there are no murmurs, bruit, etc., audible on both sides of neck. There is a faint, suprasternal pulse, a diastolic venous pulse in neck; no evidences of atheroma. Lungs anteriorly are negative; posteriorly the resonance extends an inch lower on left than on right. The breath sounds are harsher on right side, and vocal resonance more distinct; there is a to-and-fro friction sound over left base posteriorly. The lower border of liver extends about an inch below costal margin. Spleen is not palpable; no tenderness; kidneys not palpable. Knee-jerks are slightly diminished. Breath sounds are quite indistinct in expiration; markedly rhoncous in inspiration, and attended by an abundance of small frictions on right side. Feeble breath sounds at right base, with frictions.

Urinalysis. Yellow, clear; specific gravity, 1025; alkaline; albumin, sugar, bile, and indican negative. Amorphous phosphates; triple phosphate crystals.

Blood. Hæmoglobin, 95 per cent.; red blood corpuscles, 5,250,000; white blood corpuscles, 10,740.

17th. Physical signs of pleuritis and diffused bronchitis.

19th. Bronchial breathing in right base.

24th. Bronchial breathing and moist rales heard at both bases. Sore throat. Dyspnoea extreme;

sleepless; much agitation; no appetite. Sputa shows three layers, as in bronchiectasis.

25th. White blood corpuscles, 26,280. No pain. Dyspnœa and sore throat continue.

27th. White blood corpuscles, 21,480. Severe conjunctivitis. No tubercle bacilli in sputum; many diplococci. Culture from throat taken by Dr. Evans: "Growth of staphylococcus pyogenes aureus, together with bacteria, common to mouth and non-pathogenic in character. Especial attention was paid to the possibility of the presence of the bacteria of influenza and diplococcus pneumoniae, but the methods used for the growth of these failed to reveal their presence." Culture from eye: "Pure culture, staphylococcus pyogenes aureus."

28th. No tubercle bacilli in sputum; many diplococci pneumoniae. White blood corpuscles, 19,600.

31st. White blood corpuscles, 14,900. No change except aggravation of symptoms; progressive exhaustion; orthopnœa; anxiety; pain in the throat.

January 1, 1903. White blood corpuscles, 21,600. Sputum showed no tubercle bacilli on repeated daily examinations; showed diplococcus of pneumonia since December 28th, also streptococci and staphylococci. No bacillus of influenza demonstrable. Patient has coughed a great deal the last two days. Expectoration has been free, and settled in three layers in a conical glass; frothy and turbid on top, clear in the middle, and a heavy white precipitate at the bottom. The dyspnœa has increased markedly the last two days, and has been greatly aggravated by coughing spells.

2d. White blood corpuscles, 26,330. Patient spent a fairly comfortable night under the influence of frequent hypodermics of heroin. He has a constant tickling in the throat and a great dread of a coughing fit.

3d. At 4 A.M. pulse was 134 and rather weak, and his condition was that of collapse. Shortly after this time his breathing became much more labored, and he died at 5.30.

Autopsy, January 3, 1903, by Dr. R. M. Pearce.

Anatomical Diagnosis. Primary epithelial tumor of both lungs; metastasis in cervical, tracheal, and bronchial and retroperitoneal lymph nodes; fatty degeneration of liver, kidneys, and myocardium; chronic thickening of spermatic cord; cystic degeneration of thyroid; chronic splenitis; acute catarrhal bronchitis and tracheitis.

External Appearance. Body that of a well-developed, emaciated male. Old scar over left tibia. Subcutaneous fat greatly diminished in amount; muscles pale.

Abdominal Cavity. No fluid; no adhesions. Appendix normal. Retroperitoneal lymph nodes enlarged to the size of from one-half pea to one-half bean; glistening white in color; no caseation. Gastrohepatic lymph nodes somewhat enlarged in size, reaching the size of a hazel-nut, but not caseous.

Pleural Cavities. Small amount, about 50 c.c., of slightly cloudy serous fluid in either. Here and there attached to the visceral surface of pleuræ are a few fine flecks of fibrin. The lymphatics beneath the pleuræ are greatly dilated.

Pericardium. Normal amount of fluid ; surface normal except for a white patch over the right ventricle near base.

Heart. Valves and cavities normal. Myocardium soft, flabby, and on section reddish-gray in color, with coarser streaks of gray throughout.

Lungs. Uniformly throughout both lungs, affecting all parts, is a diffuse, grayish-yellow infiltration. At the periphery of the lungs this infiltration appears to a certain extent in the form of discrete areas 0.3 cm. to 0.5 cm. in diameter beneath the pleuræ. Except for this discrete peripheral distribution, the process is uniformly confluent, and exhibits a uniformly grayish-yellow, opaque appearance. Here and there are found a few older, softened areas of small size, and of a distinctly yellowish color. Bronchial and tracheal lymph nodes are enlarged to the size of a pea, smooth and glistening, and on section show no caseation.

Pancreas. Small, firm ; on section trabeculæ prominent, pulp dark red in color.

Stomach and Intestines. Normal throughout.

Liver. Capsule smooth, grayish-red in color, and on section very marked fatty degeneration of the periphery of the lobules, the centres appearing as reddish dots. Gall-bladder normal.

Kidneys. Capsule peels readily ; surface smooth. On section cortex very pale, grayish in color ; glomeruli distinct. Pyramids injected. Adrenals normal.

Bladder, prostate, and seminal vesicles normal.

Testicles and epididymis normal.

Spermatic cord shows slight glistening, fibrous thickening without, however, any evidence of tuberculosis or caseation. This condition affects both cords.

Aorta. Smooth throughout.

Organs of Neck. Esophagus normal. Trachea and larynx injected and contain a considerable amount of mucus. Glands of the neck slightly enlarged and similar in appearance to the glands elsewhere. Thyroid in the lower portion of the right lobe contains a few small cysts from 2 mm. to 4 mm. in diameter, containing clear, gelatinous material. Other portions of thyroid normal.

Head. Not examined.

Cultures from heart's blood, liver, spleen, and kidneys sterile.

Histological Description of Tissues. A superficial examination with the lower power of the microscope reveals a diffuse epithelial growth in which the general alveolar appearance of the lung is more or less retained. Areas of necrosis are not infrequent. In these areas, which are infiltrated with leucocytes, the outlines of tumor masses are still visible. In the neighborhood of such necrotic areas small accumulations of serum and fibrin are found.

Upon detailed examination the character of the tumor is found to vary in its different portions. In the younger portions, where the tumor is in contact with normal alveoli, the cells form a definite, peripheral, ring-like arrangement corresponding to the inner surface of the alveoli. These cells are in part flat, with much protoplasm and with vesicular nuclei corresponding to alveolar epithelium, and in part are pressed together to form giant-cell-like masses, with distorted and irregular nuclei. Stalk-like processes are occasionally seen to protrude into the alveolar space. Such stalk-like processes vary from those containing four, five, or six cells to large



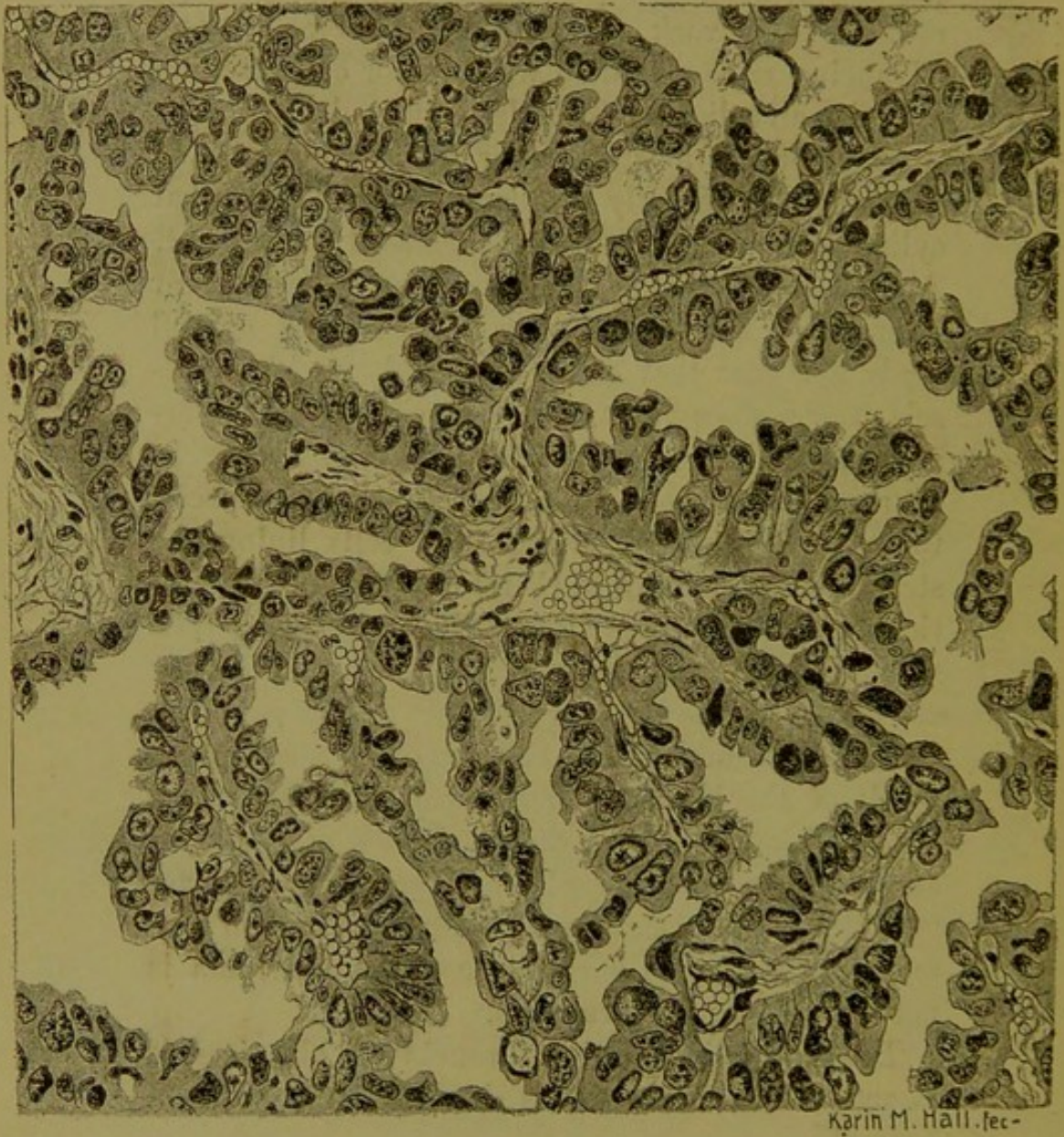
FIG. 1.—Low power. Advancing portion of tumor. Above, solid tumor with tendency to papillary arrangement; below, alveoli containing coagulated serum and small tumor masses apparently originating in epithelium of air cells.

masses completely filling alveolus. In more compact portions of tumor the cells lining the alveoli may assume a cylindrical shape. In these earlier portions of the tumor the only stroma is that of the normal framework of the lung. Alveoli along advancing edge not filled with tumor cells contain granular and disintegrated desquamated cells.

In older portions of tumor the arrangement of the tumor is distinctly papillary, the cells somewhat cylindrical, and the stroma increased in amount. At first glance this portion of tumor seems to bear no relation to the earlier portion, but on careful study it is seen that the stroma and the bloodvessels bear a close resemblance to the normal interalveolar wall. The papillary processes can, in nearly all instances, be shown to lie in spaces, their point of origin being from cells lining the stroma. The picture is, therefore, one of proliferation of cells lining the alveoli, the proliferating cells assuming, owing to the restraint under which they are placed by the limiting alveolar wall, a papillary arrangement and filling the alveolar space. As a result of the increased demand of this new tissue for nutrition, a greater vascularization of the alveolar wall has occurred with corresponding increase in stroma. The occasional presence of carbon pigment in the stroma is evidence that the stroma is not entirely a new-formation.

The epithelium lining bronchi of all sizes is intact. The mucous glands show no deviation from normal.

In loose tissue about the lymphatic spaces of the bronchi the extension of the tumor is seen in the form of a tubular arrangement of the epithelial cells entirely distinct from the cylindrical cell of



Karin M. Hall, fec-

FIG. 2.—High power, showing arrangement of cells about alveolus-like spaces and tendency to papillary growth.

the bronchial epithelium. The bronchi are filled with desquamated cells, leucocytes, serum, and red blood corpuscles.

The necrosis is of the type of coagulation necrosis, with for the most part preservation of the form of the cell; occasionally, however, complete destruction is evident. Leucocytic infiltration is extensive. Examination for tubercle bacilli gave negative results.

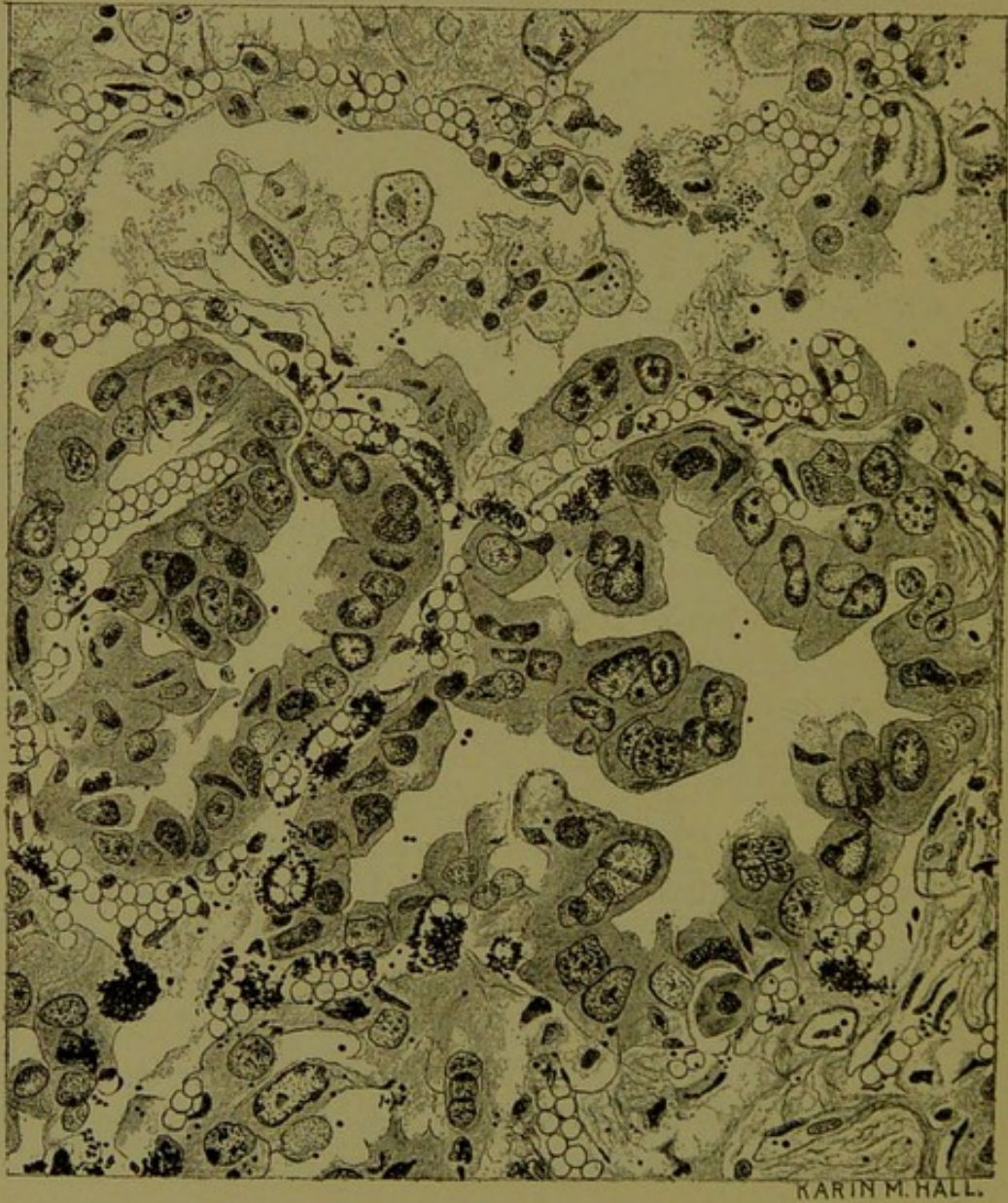
The metastases in the bronchial, tracheal, and cervical lymph nodes are of the same character as in the older portions of the tumor in the lung. The stroma is abundant, the papillary arrangement distinct, and the cells tend to take an indefinite cylindrical form. That the stroma is that of the lymph wall greatly thickened is shown by the presence of carbon pigment. Only a few islands of normal lymphoid tissue remain. In nodes most involved the growth is most abundant at the periphery, apparently extending along the sinuses toward the centre. No necrosis is seen in these metastases.

Thyroid. Examination of cystic portion of thyroid shows dilated alveoli, which are filled with colloid material. There is no atypical arrangement of the lining cells.

Spermatic Cord. Fibrous thickening about vas deferens; lumen of vas is patent, though constricted, and contains desquamated epithelial cells; the lining epithelium is quite intact.

Examination of other organs of no particular interest.

Diagnosis. Primary carcinoma of the lung originating in alveolar epithelium.



KARIN M. HALL.

FIG. 3.—High power, showing transition of cells of alveolus.

REMARKS. It was difficult for the writer to explain the *sore throat*, insomuch as the pain was out of proportion to the local lesion, and, moreover, that it was worse in the recumbent position was another phase unusual. It seemed possible there was an undemonstrable intrathoracic pressure which in some way increased the congestion and pain. Such pressure would also have explained the unusual *dyspnœa*. No other cause for the dyspnœa could be found, and no other explanation except that of miliary tuberculosis.

The very pronounced flow of mucus—the excessive *expectoration*—was a feature of great interest. Remembering well the late Dr. Harrison Allen's paper upon the occurrence of this symptom in malignant disease of the œsophagus, with intrathoracic tumor to explain the above-noted symptoms, this affection was sought, but with negative results. The only other explanation that occurred to the writer for the excessive fluid discharge was the occurrence of bronchitis due to tuberculosis. The possible occurrence of this infection seemed to explain the rapid pulse, rapid respiration, orthopnœa, emaciation, loss of appetite and of strength. The onset of signs of bronchopneumonia supported this view. The change in the physical characteristics of sputum, so that one could surmise a bronchiectasis, was in accord with this view, as such bronchial dilatation will be found in the diffused bronchitis of tuberculosis. Against tuberculosis was the negative findings on examination for bacilli. (The guinea-pigs did not succumb to tuberculosis, although sufficient time after inoculation had not elapsed to make this a diagnostic point.) If the writer had maintained that tuberculosis was not

proven as bacilli were not found, no positive diagnosis would have been made. The clinical course, the rapid progress, the rapid pulse, the thoracic symptoms and signs, it seemed to the writer, could alone be explained by this infection.

The diagnosis of carcinoma of the lung was not made for the reasons mentioned. In the light of the autopsy we can now explain the symptoms which were out of proportion to physical signs, early at least in the affection. The rapid breathing, the rapid pulse, the severe orthopnoea, the excessive expectoration, all had their origin in the diffused lesion with which we were confronted at the autopsy. Stenosis of the smaller divisions of the bronchi was produced by the great epithelial proliferation.

Of interest, too, during life was the enlarged thyroid, which proved to be cystic, suggesting an explanation for the rapid pulse.

It may be noted that the cases herein reported swell the large proportion of males to females already commented upon by writers.

Finally, it may be worth recording, had we put more faith in the examination of the sputum, which always was against tuberculosis, we would have at least not made a positive diagnosis from which there was no retraction.

On the other hand, too much stress in both cases was placed upon the *leucocytosis*. Not that its presence counted for or against tuberculosis, the latter in uncomplicated cases. Here, indeed, it could be said the leucocytosis was against tuberculosis, which should have some weight, although we held, and it was no doubt true, the blood change was due to a mixed infection. In the first instance the increase

of white cells in a supposed pleural infection was thought to be due to a small empyema, perhaps on the diaphragm, upheld for a long time by the clinical course.

To summarize, it may be said the case is of interest because—

1. Of its rarity.
2. The complete clinical and pathological study.
3. The apparently simultaneous involvement of almost the entire extent of *both* lungs (almost complete involvement of one lung is not uncommon).
4. Evident origin from epithelium of alveoli. Most of the cases described in the literature have arisen in bronchial epithelium. Very few (see Nothnagel) writers ascribe origin to alveolar epithelium. The illustrations (high power) are an attempt to demonstrate this origin.

