CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 4-1967

PRESENTATION OF CASE

First admission A sixty-three-year-old man entered the hospital because of a head injury and for investigation of progressive dyspnea.

Three weeks previously, when he came home from his office, a lump and some blood on the back of his head were observed. He was unable to relate what had happened and subsequently appeared normal except for a slight decrease in hearing. There was no history of tinnitus, dizzy spells, headache, loss of consciousness, seizures, weakness, paresthesias or difficulty with locomotion or speech.

For several years he had been dyspneic, with a chronic cough productive of up to 30 ml. of mucoid, blood-free sputum daily. The dyspnea increased in severity shortly before admission, to the point that he was unable to climb more than 2 flights of stairs without stopping. He had had no pain or discomfort in the chest or pulmonary infections. He had smoked 2 packages of cigarettes daily for forty years. During the year before entry he lost about 15 pounds in weight. There was no known exposure to tuberculosis.

He had been employed for twenty-five years as a letter carrier and had previously worked for thirteen years as a painter and for five years as a riveter. Thirty-five years before admission he had worked for two years on the construction of coke silos. From the age of eighteen to twenty-three years he had been a boxer. For four years there had been swelling and restriction of motion in the joints of the fingers.

Physical examination revealed a pale, slightly cachectic man with an abrasion over the left occiput. The cervical veins were flat. Multiple rubbery lymph nodes, 1.0 to 1.5 cm. in diameter, were palpable in the right and left supraclavicular areas and in each axilla, and a firm, round nodule, 3.5 cm. in diameter, was felt over the costal cartilage of the right second rib. The anteroposterior diameter of the chest was increased, and the lungs were hyperresonant. There was severe limitation of movement of the right hemithorax, and the diaphragmatic excursion was estimated to be less than 2 cm. The breath sounds were of poor quality, and the expiratory phase was prolonged, with expiratory wheezes and coarse rhonchi. The cardiac impulse could not be felt; there was no murmur or friction rub. The edge of the liver was felt 2 fingerbreadths below the right costal margin. Slight clubbing of the fingers and toes and cyanosis of the nailbeds were observed. Neurologic examination was negative.

The temperature was 98°F., the pulse 72, and the respirations 25. The blood pressure was 110 systolic, 60 diastolic.

The urine was normal. The hematocrit was 38.5 per cent; the white-cell count was 8000, with 74 per cent neutrophils. The erythrocyte sedimentation rate was 46 mm. per hour. The glucose was 77 mg., the urea nitrogen 15 mg., the calcium 9.4 mg., the phosphorus 3.6 mg., and the protein 7.0 gm. (the albumin 3.7 gm., and the globulin 3.3 gm.) per 100 ml. The alkaline phosphatase was 7.2 Bodansky units. Serum electrophoresis showed that the albumin was 43 per cent, the alpha$_1$ globulin 9 per cent, the alpha$_2$ globulin 13 per cent, the beta globulin 17 per cent, and the gamma globulin 18 per cent. Examination of a specimen of arterial blood revealed that the partial pressure of oxygen was 63 mm. of mercury, the partial pressure of carbon dioxide 47 mm. of mercury, and the pH 7.44. The glutamic oxalacetic transaminase (SGOT) was 10 units. The

FIGURE 1. *Posteroanterior Film of the Chest, Revealing Thickening of the Pleura in the Right Hemithorax.*
Calcification is visible in the pleura overlying the left diaphragmatic leaf (arrow).

and "Give us more money" becomes the refrain of the profession. Furthermore, the universal exchequer financing of the service endows everyone providing it with a vested interest in denigrating it, so that it presents the unique spectacle of an undertaking that is run down by everyone engaged in it.

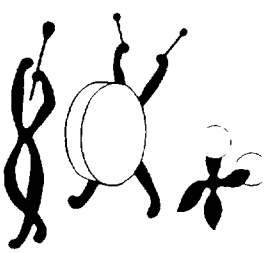
He admits that it is because medical care under the National Health Service is rendered free to the consumer at the point of consumption that supply and demand are not kept in balance by price. Indeed, the demand, for all practical purposes, is unlimited, and with every new development in treatment it tends to increase. On the other hand the supply is limited by governmental action through the parliamentary votes for the National Health Service and in the hospital service, the Minister of Health then decides how much each hospital board shall be allowed to spend each year. There is thus in effect a rationing system of medical care determined by political expediency. On the other hand Mr. Powell points out that the public is encouraged to believe that rationing in medical care was banished by the National Health Service and that the very idea of applying rationing to medical care is immoral and repugnant. Nevertheless, waiting times for clinic appointments and waiting lists for admission are obvious manifestations of a rationing system. But, again, Powell points out that the necessity for these covert forms of rationing springs from "Parkinson's law of hospital beds," which asserts that the number of patients always tends to equality with the number of beds available for them to lie in, and he admits that even given the insight and the will to do so, the politicians could not alter this law.

Turning to the differing points of view of the politician and the doctor Mr. Powell recognizes that by tradition and training, the doctor upholds the independence of individual professional judgment and accepts responsibility for each patient whereas the politician is concerned with the general consequences of individual decisions. Furthermore, he points out that in all governments the decisions of policy must be taken by the layman.

There is no doubt that Powell himself does not believe that apparently free medical attention at the time of need is the right method of providing a national health service. Indeed, he concludes that a change in the relation of medicine and politics will only be heralded when the number of family doctors and the volume of consultation and hospital treatment tendered outside the National Health Service shows a marked and continuing rise (and it will be noted that this is quite the reverse of Professor Miller's view).

Nevertheless, the tragedy of Mr. Powell's critical appraisal of the present situation is that although clearly an expert diagnostician, he can offer no treatment, admitting in his final sentence that he has pursued an argument in a circle — "the circle in which Medicine and Politics are imprisoned in the National Health Service."

Expressed in other words the tragedy seems to be that the doctors and the politicians are running on parallel lines that will never meet, but if they do not, the patients will eventually be the losers.



rheumatoid factor was positive at a dilution of 1:32. Tests of pulmonary function revealed a vital capacity of 2.3 liters (56 per cent of the predicted value), with a one-second vital capacity of 1.2 liters; the maximal breathing capacity was 20 liters per minute (15 per cent of the predicted value). Cytologic examination of the sputum was negative. An electroencephalogram was normal. Lumbar puncture yielded clear cerebrospinal fluid under a pressure of 180 mm.; the fluid contained no cells; the protein was 32 mg. per 100 ml. An electrocardiogram demonstrated a sinus tachycardia and low voltage; there was no evidence of right ventricular hypertrophy. X-ray films of the chest (Fig. 1 and 2) revealed a slight reduction in volume of the right hemithorax, with diffuse pleural thickening along the right hemidiaphragm and lateral chest wall; a few plaques of calcification were seen in the thickened pleura; the right hemidiaphragm could not be visualized. Multiple rounded densities, the largest approximately 10 mm. in diameter, were visible in the right-lung field. The left-lung field appeared clear, but increased linear markings were evident, and there were calcified plaques overlying the diaphragm on the left side. The heart was not enlarged. Incomplete fractures of the left sixth and seventh ribs anteriorly were demonstrated; the adjacent bone appeared normal. A barium-swallow study (Fig. 3) showed indentation of the esophagus below the carina. Films of the skull were of poor technical quality; a fracture was not identified.

Bronchodilators and antibiotics were administered, with slight improvement of the dyspnea. The patient was discharged on the twelfth hospital day.

Final admission (three weeks later). He remained well until two days before entry, when his sister heard him cough and then fall; she found him dyspneic but alert. On the morning of admission he was again heard to fall to the floor and found with blood coming from his nose. A seizure was not observed, and he appeared alert. He denied chest pain or hemoptysis.

Physical examination showed a man in moderate respiratory distress, with cyanotic nailbeds and clotted blood in the left nostril. Examination of the chest and abdomen and neurologic examination revealed no change.

FIGURE 2. *Detail of an Oblique View of the Right Lateral Thoracic Wall, Showing a Thick Nodular Pleura (Arrows).*

FIGURE 3. *Detail of an Oblique View of the Barium-Filled Esophagus, Showing Indentation Just Below the Carina.*

The temperature was 98.6°F., the pulse 120, and the respirations 24. The blood pressure was 140 systolic, 90 diastolic.

The urine was normal. The hematocrit was 38 per cent. The sodium was 148 mEq., the potassium 4.9 mEq., the chloride 102 mEq., and the carbon dioxide 24 mEq. per liter. The urea nitrogen was 17 mg. per 100 ml. An electrocardiogram showed a sinus tachycardia, with low QRS voltage and minor T-wave flattening. An x-ray film of the chest showed no change.

The patient was increasingly dyspneic and had difficulty raising tracheal secretions. The neck veins became distended, and a diastolic gallop was heard. Digoxin and meralluride were given. Early in the morning of the second hospital day he was found dead on the floor of his room.

Differential Diagnosis

Dr Felix G. Fleischner*: We are discussing a man of sixty-three years with chronic pulmonary disease. We hear of considerable cigarette smoking and are given a fairly thorough vocational history. I am glad that the questioner did not stop with the job of letter carrier for twenty-five years, but probed further and discovered the patient's thirteen-year activity as a painter and two years in construction work. Incidentally, I inquired at our State Health Services and learned that the building of coke silos entails no particularly harmful exposure.

The physical findings in the chest seem to confirm the impression that he had chronic pulmonary disease – namely, chronic bronchitis and emphysema. The clubbing of the fingers and cyanotic nailbeds are also nonspecific changes, consistent with any type of chronic bronchopulmonary disease with oxygen desaturation. The slight elevation of the rheumatoid factor is nonspecific, too, and could have resulted from any type of granulomatous process in the lung. The laboratory studies disclosed moderate anemia and a markedly elevated sedimentation rate in the absence of tuberculosis or any other known inflammatory disease. The alkaline phosphatase level was high, and the question arises whether it points to bone involvement of some kind. Considerable arterial oxygen desaturation and slight hypercapnia were found. The marked reduction in the vital capacity and reduction in the timed capacity demonstrated by the pulmonary-function tests were indicative of emphysema of the obstructive type. We have no other information that would enable me to say anything about diffusion impairment and venous admixture, both of which were probably present.

I come, then, to the radiologic findings. Although the films of the skull are of poor technical quality, I can detect a fissure fracture on the left side extending through the occipital squama, coinciding with the location of the lump and the abrasion incurred three weeks before the first admission. I regard that lesion as incidental, however, since we have been assured that the neurologic examination was negative on both hospital admissions. The films of the chest (Fig. 1) show overall symmetry, but we see some narrowing of the intercostal spaces on the right side, and the mediastinal structures are displaced to the right. There is an opacity in the right-lower-lung field, but I cannot distinguish how much of it is pleural and how much pulmonary consolidation. Numerous streaks and flecks are evident in the right lung. In addition, there are multiple dense, round lesions that might be characterized as "doughnut-like" since they have translucent centers. Such lesions have been described as "button-shaped," and their appearance stigmatizes them as pleural calcific plaques rather than nodular pulmonary lesions. On the left side, in addition to the two rib fractures, we find only a few streaks and one nodular lesion of a nondescript nature, otherwise, the left lung is clear. Perhaps the most important finding in this whole analysis, although it is not very prominent, is the presence of calcification in the region of the diaphragmatic pleura on both sides. In an attempt for better definition of the palpable firm lymph node in the right infraclavicular region oblique views were taken. They reveal numerous soft-tissue masses in and about the pleura, with some nodularity extending into the pulmonary tissue (Fig. 2). There is a cortical defect in the anterior portion of the second rib on the right side that corresponds to the area where the hard nodule was palpated. The nodule, although indolent and firm, did not contain calcium or bone. Another oblique view of the chest with barium in the esophagus (Fig. 3) again demonstrates the anterolateral pleural deposits, but I wish to call attention to the indentation of the esophagus just below the bifurcation of the trachea, which is a very important finding. It is not just a peristaltic wave. On careful scrutiny one can see a soft-tissue mass that fills the bifurcation angle and compresses the right main bronchus. This alteration signifies marked enlargement of the bifurcation lymph nodes, presumably by tumor.

The x-ray films demonstrate, therefore, signs of pulmonary fibrosis in the form of strands and flecks, a nodule on the left side, presumably of the same nature, and localized bone involvement. These changes are in no way characteristic. Fibrosis occurs with many conditions, including several types of pneumoconiosis, and rarely has any distinguishing features. The old-time descriptions such as a "hazy groundglass appearance" and a "shaggy heart shadow," used in cases of asbestosis, belong to an abandoned vocabulary. I have deduced already that there was a malignant tumor in the chest on the basis of the deposits in the pleura and the mediastinal lymphadenopathy. The problem is how to connect the chronic pulmonary disease and the malignant pulmonary or pleural lesions in this patient

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In my opinion, the bilateral calcification of the diaphragmatic pleura is the key to the diagnosis. Calcification in a thick pleural scar was a relatively common finding formerly and is still seen from time to time after empyema, tuberculous and other pleural effusions and traumatic hemothorax. In such cases it occurs usually at the mid-level of the chest, and in a large survey it was found that in 97 per cent of the cases the pleural calcification was unilateral if it was associated with a hemothorax or empyema. In most cases of asbestosis, on the other hand, the calcification is bilateral and is usually in the lower portion of the chest, in the costal pleura, the diaphragmatic pleura or the mediastinal pleura. In this case we find bilateral diaphragmatic calcification. Pleural calcification has also been described in association with silica and talc pneumoconiosis. It is possible that there was an admixture of asbestos in those cases.

A few general remarks about asbestos and asbestosis are in order. Asbestos is composed of several chemical compounds — silicates of iron, magnesium and aluminum. The fibers are separated from crushed rock. The ancient Egyptians, Greeks and Romans definitely knew about the nature of asbestos; in fact, Plutarch tells about its use as the perpetual wick in the lamps of the Vestal Virgins. Recent archeologic discoveries in Finland, where much asbestos is still mined, showed that the Stone Age man used asbestos, more than six thousand years ago. We are interested in asbestos because of its extensive utilization in modern industry, being woven into textiles and ground and mixed with cement and plastics to make insulating materials and other products. Asbestosis has been known medically for about three decades. The dust is inhaled in a fibrous form. When the serious nature of massive inhalation was first realized the fibers used were about 200 μ in length, but much shorter fibers, 2 to 5 μ, are employed now. There is some evidence that the inhalation of the shorter fibers is changing the nature of the disease and making it more chronic. In the earlier days asbestosis developed after only two or three years of exposure and often ended fatally within that period. The pulmonary lesions differ from those of silicosis. Observations in man and experiments with animals in the early phase of the disease have shown bronchiolitis, with extension of the inflammation into the adjacent alveoli.[1] At a later stage widespread, progressive fibrosis of the lungs develops, with involvement of the adenoid structures. The inhaled dust soon becomes coated with iron-containing protein to form asbestos bodies, which are said to be indestructible. Radiologically, the disease is characterized by signs of diffuse interstitial fibrosis, without grossly visible nodularity, occupying mainly the lower lung fields. The picture is sometimes very similar to the alterations seen in cases of scleroderma.

Involvement of the pleura is very common in cases of asbestosis. For example, in a series of 24 patients with asbestosis 19 proved to have pleural involvement.[2] Kiviluoto,[3] a Finnish radiologist who studied the disease among workers in open-air mining, advanced an interesting theory regarding the pathogenesis of the pleural involvement. He postulated that the asbestos fibers or needles penetrate the lung surface and with the respiratory up-and-down movement scratch the parietal pleura, causing minute hemorrhages, with subsequent fibrin deposition, organization and eventually calcification. There are certain unusual characteristics. In a large calcification due to an old empyema one generally finds the shell of calcium at some distance from the ribs, whereas the calcification due to asbestosis always lies close to the ribs. Another interesting feature of this disorder is that despite the presence of calcification there frequently are no pleural adhesions. One can successfully induce a pneumothorax, and the pathologists often find no adhesions, in contrast to the obliteration of the pleural space by postempyema scars. It takes a long time for the pleura to become calcified. Calcification is an extremely rare finding in people who were exposed to asbestos less than twenty years previously. The intensity and duration of exposure does not seem to be significant in this regard, but if the exposure to asbestos dates back thirty or forty years the likelihood of finding pleural calcification is fairly great.

It also takes a long time for the asbestos to manifest its carcinogenic quality. The most important aspect of this disease is the fact that the asbestos acts as a carcinogen. In a recent review of 307 deaths among asbestos-insulation workers in New York and New Jersey, Selikoff and his co-workers[4] reported that 53 had bronchogenic carcinoma, 34 had cancer of the stomach or colon, and 10 had a malignant mesothelioma of the pleura or peritoneum. Dr. Knowles discussed a similar case at one of these conferences three years ago.[5] The urgency of the problem recently led to a conference of the New York Academy of Sciences on the subject of the biologic effects of asbestos, and the ensuing volume[6] contains practically everything that is known about asbestosis as well as numerous questions about unsolved aspects of the disease. Included in the data is a list of all the occupations in which one can contract asbestosis, compiled by Hueper,[7] from the National Cancer Institute, in Bethesda, Maryland. Among them are mining, loading, shipping, crushing, milling and other ways of handling this mineral, as well as spraying of steel construction, the undercoating of automobiles and insulating pipes and handling of the filler in rubber goods and pipe coverings, insulation blocks and insulation jackets. However, nonoccupational asbestosis is of particular interest. Kiviluoto[3] first used that term when he discovered that the air in the mining area in Finland was so polluted that even cattle contracted asbestosis. We now have a new term, "residential" asbestosis, and among those exposed, for example, are people who live along

roads on which asbestos is trucked and inhabitants of houses with asbestos insulation. Asbestosis no longer is a rare occupational disease of interest only to the physician who deals with workers in asbestos mines and mills and with insulation, construction or demolition workers and pipe fitters. It concerns virtually everyone. In the last ten or fifteen years the use of asbestos has multiplied geometrically, in width of usage and in depth of amount. The abrasive dust from the lining of the brakes of our cars, from tiles, from house paint and from a hundred other sources pollutes our air. A pathologist in Belfast, North Ireland, has declared that a fourth of the population in that region has nonoccupational, residential asbestosis of sufficient degree to pave the way for the development of neoplasia, the representative speaker of the Ministry of Health in London has stated that in more than half the fatal cases of asbestosis some kind of cancer is present, and Thomson and Graves,[8] in Miami, Florida, found asbestos bodies, admittedly in a small number, in the lungs in 20 to 30 per cent of 500 consecutive autopsies. The general contamination of the urban atmosphere by asbestos has obviously become a matter of public concern.

I must return to the case at hand and arrive at a diagnosis. On the basis of the vocational history, the increasing dyspnea accompanied by chronic bronchitis and clubbed, cyanotic fingertips and the radiologic findings in the lungs and particularly the bilateral pleural calcifications in the lower portion of the chest, the diagnosis of asbestosis of the very chronic type is justified. The recent deterioration of the patient's condition, with weight loss and anemia, suggests a wasting disease. Against the background of long standing asbestosis, a malignant tumor in the chest is a cogent conclusion. The question is whether it was a bronchial carcinoma or a malignant mesothelioma of the pleura. I think that a malignant lymphoma can be ruled out. In favor of the diagnosis of a bronchial carcinoma is the observation of partial bronchial obstruction in the right lower lobe. That is not absolute proof, however, since obstruction or even invasion often occurs as a result of involvement of lymph nodes by metastases. The absence of hemoptysis and the negative cytologic studies provide a fairly strong argument against a bronchogenic carcinoma. In favor of a primary pleural tumor are the obvious pleural involvement by tumor and the negative arguments for a bronchogenic carcinoma. Against a pleural tumor is the statistical probability. According to the latest figures by Selikoff et al.[4] the odds are about 5 to 1 – that is, 5 bronchogenic carcinomas to 1 mesothelioma of the pleura or peritoneum.

My conclusion is that the patient had asbestosis, with pulmonary fibrosis, chronic bronchitis, emphysema and bilateral pleural calcification. He had a malignant pulmonary or pleural tumor, with mediastinal lymphadenopathy and extension into the second rib on the right side. Disregarding statistical probability and resting my case more on roentgenologic evidence, I give a malignant pleural mesothelioma slight diagnostic preference over a bronchial carcinoma. I have too little supporting evidence to say whether the fracture of the occipital squama or a metastasis to the brain contributed to this man's death.

DR. JOHN H. KNOWLES: I'd like to ask two questions, Dr. Fleischner. Is it possible for a boxer to suffer severe rib fractures during boxing matches over a period of years sufficient to cause multiple calcifications of the pleura on both sides of the chest?

DR. FLEISCHNER: There might be calcification if he had a bilateral hemothorax forty years ago, but it would be a far-fetched explanation for the extensive calcifications principally in a diaphragmatic location in this case.

DR. KNOWLES: Secondly, how do you account for the abruptness of the terminal event?

DR. FLEISCHNER: The tachycardia, diastolic gallop and engorgement of the neck veins indicate that there was myocardial failure at the end. The roentgenograms of the chest show some haziness that is probably indicative of pulmonary congestion. Therefore, I assume that the final event was congestive heart failure. Whether the head injury or a cerebral metastasis or some other factor contributed to it, I do not know.

DR. BENJAMIN CASTLEMAN: Dr. Knowles, do you agree with Dr. Fleischner's conclusion that this man had a mesothelioma of the pleura on the basis of asbestosis?

DR. KNOWLES: Yes, I would have come to that diagnosis.

DR. CASTLEMAN: Dr. Bird, you followed this patient in the hospital. Will you comment on your thinking about the problem?

DR. KENNETH T. BIRD: As I recall, I related the abnormalities of the right pleura to the history of a few years spent as a boxer.

DR. CASTLEMAN: In the record you listed your diagnostic impressions as the chronic bronchitis syndrome, rheumatoid lung disease and pleural fibrosis and calcification, secondary to either boxing trauma or rheumatoid disease.

DR. BIRD: I don't think there's enough in the history to let us do more than speculate freely about the diagnosis of asbestosis. We have only the fact that the patient worked for thirteen years as a painter. We have been concerned recently by the high incidence of asbestosis among ship workers.

DR. CASTLEMAN: I just noticed an addition to this man's occupational history. He passed rivets for two years, from 1919 to 1921, then heated rivets for three years, 1921 to 1924, and painted from 1924 to 1937, but during the entire period from 1919 to 1937 all this work was done at a shipyard. Does that change your mind?

DR. BIRD: That history was obtained by me with the courtesy and help of the patient and his sister.

and I must say that I completely overlooked its possible significance. It's extremely unusual, however, for asbestosis to present primarily as a unilateral disease. We are currently participating in a survey of 160 pipe coverers, about 20 of whom have asbestosis, and all of them have bilateral disease.

DR. FLEISCHNER: As to the question of the asymmetry of this man's thoracic disease, the asbestosis still could have been bilateral and symmetrical. The unilateral appearance is probably due to the development of a malignant tumor on the right side. Incidentally, the elevated rheumatoid factor should not mislead us. That is a nonspecific alteration that occurs in association with lupus erythematosus and other collagen diseases, and Selikoff and his associates found elevation of the rheumatoid factor also in cases of asbestosis.

DR. GILBERT S. OMENN: In view of the cyanosis and the arterial oxygen desaturation in this case, the hematocrit of 38.5 per cent was probably significantly lowered. Would you postulate bony metastases to account for it, Dr. Fleischner?

DR. FLEISCHNER: I suspect that there was more bone involvement than is evident in the right second rib. The elevated alkaline phosphatase level can probably be explained on that basis.

DR. ANTONIO M. GOTTO, JR.: I might add that I saw the patient on the night before he died. We were very puzzled by the two spells of falling that prompted the last admission. Earlier in the day, at the time of admission, the examiners did not find evidence of congestive heart failure. However, at eleven o'clock at night when I made rounds I found him dyspneic, with distended neck veins and a gallop rhythm, and we began digoxin and meralluride. Three hours later he was found on the floor of his room by the nurses. Somehow he had managed to get out of bed, and we assumed that he had had another similar spell, whatever its nature. We had a long attempt at resuscitation, but it was not successful. Dr. Fleischner, do you think that there could have been cardiac involvement by the mesothelioma? Are the electrocardiograms or any of the terminal findings consistent with involvement of the heart?

DR. FLEISCHNER: That is definitely a possibility, and I did think of it. Whenever one suspects a malignant tumor of any kind in the chest one should look for a rapid increase in the cardiac silhouette, which serves as a warning that the tumor has probably extended or metastasized to the pericardium from mediastinal lymph nodes, causing a pericardial effusion. Solid encasing by tumor is much rarer. However, on the latest films in this case the size and shape of the heart were entirely proportionate and even on the small side, and so I couldn't come to such a conclusion.

DR. WILLIAM FRANKLIN: I wonder if the spells of falling were due to cough syncope in a person with chronic bronchitis and obstructive pulmonary disease.

DR. FLEISCHNER: I thought of spells of carbon dioxide intoxication.

DR. CASTLEMAN: What conclusion did the students reach?

DR. WILLIAM J. POWELL, JR.: The majority of the students thought that the patient had a primary bronchogenic carcinoma, chronic bronchitis and emphysema. Mr. Meissner was the student discusser today.

MR. WILLIAM MEISSNER: My diagnosis was primary bronchogenic carcinoma, either of diffuse origin or possibly of bronchiolar origin. My second choice was a mesothelioma of the pleura.

CLINICAL DIAGNOSES

Chronic obstructive pulmonary disease, with fibrosis.
Bronchogenic carcinoma.
? Pulmonary embolus; ? myocardial infarct.

DR. FELIX G. FLEISCHNER'S DIAGNOSES

Asbestosis, with pulmonary fibrosis, chronic bronchitis, emphysema and pleural calcification, bilateral.
Mesothelioma of right pleura, ? with metastasis to brain.
Fracture of occipital squama.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The post-mortem examination revealed that the entire right pleura was thickened and replaced by tumor that involved the parietal as well as the visceral portions, with no pleural space remaining. The tumor also involved all the mediastinal structures, including the parietal pericardium, and had compressed both the superior vena cava and the inferior vena cava. The right lung was completely encased by a layer of tumor with a thickness of several centimeters (Fig. 4). Therefore, this man had a very extensive pleural tumor that involved part of the pulmonary parenchyma, but only by extension and not by lymphatic spread. Calcification was evident in both the right pleura and the diaphragmatic portion of the left pleura. The tumor was adherent to the inner surface of the thoracic wall, with some extension into the periosteum of the ribs, but it did not actually invade the rib marrow (Fig. 5). The pericardial cavity contained about 300 ml. of reddish-brown fluid, and the epicardium was covered with fibrin and small tumor nodules (Fig. 6). The right ventricle was three times the normal thickness. That change apparently was not reflected in the electrocardiograms, perhaps because the cardiac chambers had been rendered virtually immobile. Histologically, the tumor was a fibrous type of mesothelioma in many areas (Fig. 7); in other areas, however, we observed the pseudoacinar and papillary arrangement, with cuboidal mesothelial cells, that is more characteristic of the mesothelioma (Fig. 8).

FIGURE 4. *Posterolateral View of the Right Lung Encased by White Fibrous Tumor, Also Involving the Pleura, Mediastinum and Pericardium.*

FIGURE 5. *Tumor Involving the Inner Surface of the Anterior Chest Wall.*

In the diaphragm on the left side there was dense, acellular fibrosis, with a plaque of calcification 2 or 3 mm. in thickness and 4 cm. in diameter (Fig. 9). As Dr. Fleischner intimated, when a patient has bilateral calcification of the pleura, especially involving the diaphragm, the burden of proof rests on the person who says that it is not due to asbestosis. In fact, Selikoff[9] stated that when there is bilateral pleural calcification of this nature involving the diaphragm the cause is invariably asbestosis,

FIGURE 6. *Epicardium Replaced by Tumor and Fibrin, with Underlying Normal Myocardium. (X36)*

FIGURE 7. *Mesothelioma, Predominantly Fibrous. (X200)*

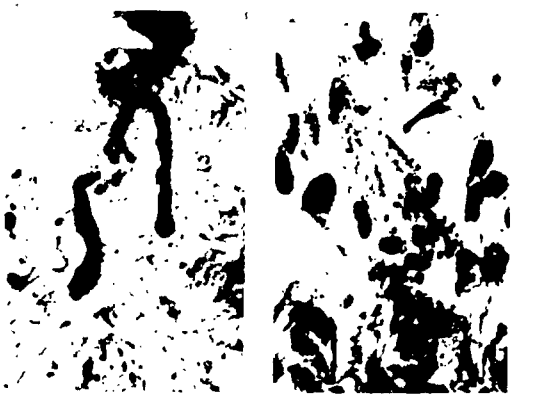
and it's up to the examiner to find the asbestos bodies. One almost never can detect asbestos bodies in the thickened pleura, and it's very rare to spot them among the tumor cells; the place to look for them is in the pulmonary parenchyma. Therefore, we made many sections of the lungs in this case. There was

FIGURE 8. *Mesothelioma, Composed of Both Spindle-Shaped and Cuboidal Cells in a Papillary Arrangement (X160).*

FIGURE 9. *Diaphragm Replaced by Dense, Acellular Fibrous Tissue. (X37).*

A focus of calcification is evident.

only slight chronic bronchitis, with minimal fibrosis. I looked very carefully for asbestos bodies, especially in areas where there was carbon, which sometimes covers up a fragment of asbestos, but was unsuccessful. I then sent some of the material to Dr. Irving J. Selikoff and Dr. Jacob Churg, to whom I turned for consultation because I was convinced that this patient had asbestosis. The best way to detect asbestos bodies is to ash the tissue, since everything will burn out, with the asbestos body remaining. They very kindly undertook that procedure for me, and I received from them this morning several lantern slides disclosing asbestos fibers. One photograph was taken of the squeezed-out lung, showing an uncoated fiber, and others, which were of the ashed specimen, revealed clear-cut asbestos bodies (Fig. 10). There is no question that this patient had asbestosis.



A B

FIGURE 10. *Asbestos Bodies from the Ashed Lung.*

The clubbing of the asbestos body is well seen in A, and the fragmentation in B.

This man proved to have a large subdural hematoma, dating back two months to the trauma to the head. The subdural hematoma may have accounted in part for the spells of falling.

ANATOMICAL DIAGNOSES

Mesothelioma of pleura, right, with extension into mediastinum, chest wall and pericardium.
Pulmonary asbestosis.
Pleural fibrosis and calcification, bilateral.
Cor pulmonale.
Subdural hematoma, chronic.

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INFORMATION EXCHANGE

WHEN the six-year experiment of the National Institutes of Health with seven Information Exchange Groups (IEG) ends in March, many scientists will be without a means of communicating their ideas rapidly among colleagues in research. Private circulation of preprints to a limited circle of senior investigators will doubtless be resumed, and distinction will again be drawn between the privileged few who know the latest data from other laboratories and the unenlightened masses.

Why did the IEG succumb? In principle their operation was simple enough. All that was required of the participants was that they send copies of their manuscripts or of their informal memos to Bethesda, and soon photo-offset copies would go out to an international membership at no cost to the participants.

Two things happened to mar the beauty of this operation. First, in the areas of immunology and of nucleic acids, the contributions became so numerous that it took two or three months before copies could be made. Manuscripts submitted to *Science*, *Biochemical and Biophysical Research Communications* and *Proceedings of the National Academy of Sciences* appeared in print before the IEG papers were mailed. Second, some authors incorrectly inferred that they were being asked to establish priority by submitting papers to the IEG immediately on their completion. The implications that the established referee and publication system would be circumvented were not lost either on morally sensitive scientists or on editors of journals themselves. An appreciable number of immunopathologists voted to abandon their IEG. *Nature* devoted a long leading article to the defects of the system and suggested that the $5,000,000 ultimately needed to extend the IEG to all areas of research supported by the National Institutes of Health could better be spent to improve the quality and speed of publication of existing journals. Furthermore, it pointed out, scientists invariably know by word of mouth the important unpublished research in their field.

Spoken and applied to leading scientists in nonclinical fields in major institutions, the criticisms were true, but they ignored both the scientist whose institution is not a Mecca and the physician in laboratory medicine. Unless the physician had abdicated clinical medicine, he was unlikely to belong to a select scientific clique. Irrespective of the importance of new data to his research, he would not know the content of privately circulated preprints until they actually appeared in journals. Delays of more than a year in publication meant that he was at least two years removed from the creativity of his fellows in basic science.

The IEG's should have been encouraged as a means of relieving this situation. Clearly, the mission of the NIH includes any measures that will enable investigators in biomedical fields to know

ASBESTOSIS

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL: CASE 4-1967

B. Castleman, M.D. and B. U. McNeely