

were
itous.

le sug-
lustra-
ndered
express
(Can-
supply

O 241,

shed by

34 201,

35 56,

PULMONARY ASBESTOSIS

V. A REPORT OF BRONCHIAL CARCINOMA AND EPITHELIAL METAPLASIA ¹

KENNETH M. LYNCH, M.D., AND W. ATMAR SMITH, M.D.

*(From the Departments of Pathology and Medicine, Medical College of
the State of South Carolina)*

Following our report in 1935 (1), some further interest in the occurrence of lung cancer in asbestosis has been manifested. Six cases have been recorded, by Gloyne (2, 3), Egbert and Geiger (4) and Nordmann (5). The present report brings the total to 8. Nordmann believes that these cases should be classified as occupational cancers.

In 1938 Anderson and Dible (6) studied the silica content of the lungs and the histologic evidence of pneumoconiosis in 70 persons who died of pulmonary carcinoma and in 50 non-cancer subjects. A greater incidence of silicosis and a greater lung silica content were found among those who had cancer than in the control series, from which the authors conclude that the rôle of the silicosis is etiologic.

Vorwald and Karr (7), also in 1938, reviewed the reports of carcinoma of the lungs in subjects of pulmonary dust disease and reached the conclusion that no relationship has been shown between the inhalation of dust and the occurrence of cancer and that, except as it contains known carcinogenic factors, such as tar or radium, dust cannot be considered as of etiologic significance in malignant disease of the lungs.

In 1939 Klotz (8) reported that from 1925 to 1936 there occurred in his necropsy service 50 cases of silicosis, among which were 4 instances of bronchiogenic carcinoma, an incidence of 8 per cent, while in his total of 4500 necropsies for that period there were 53 primary cancers of the lung, an incidence of only 1.18 per cent.

It was soon after reporting the first case that the writers encountered a second.

A white man first presented himself in the dispensary at the age of forty-two. He had then been employed as a weaver in an asbestos mill for seven years. His complaints were shortness of breath and lassitude. No other significant symptoms were elicited. There were somewhat diminished expansion of the left chest and dullness in the left axilla and in the right base posteriorly. A few râles were heard in these areas and in the upper right axillary region and the left base posteriorly. The roentgen report at that time is as follows: "Bronchial lines slightly heavier in the left chest but not sufficient to warrant a diagnosis of tuberculosis." No tubercle bacilli were found in the sputum and serologic tests for syphilis were negative.

The patient was not seen again until six years later, when he was complaining of shortness of breath and soreness in the chest. He had continued to work in the asbestos mill, giving him a total of thirteen years' exposure to asbestos dust. He stated that he had been gradually becoming weaker, more easily fatigued, and shorter of breath for about two years, and had developed a cough, productive of thick phlegm but no blood. For about a year he

¹ Read before the American Society for Cancer Research, Richmond, Va., April 5, 1939

had experienced pain in scattered areas over the chest. At this time he had stopped work on account of weakness. He had lost ten or twelve pounds in weight in the last few years.

After thirty days in the hospital the patient was discharged, having shown progressive improvement. During his hospital residence his temperature remained normal, his pulse varied from 80 to 110, respirations ranged between 20 and 30, and the blood pressure was around 142 systolic and 96 diastolic.

At this time chest expansion was diminished bilaterally, tactile fremitus was alike over the two sides, and no abnormal areas of dullness were found. The breath sounds were



FIG 1 LUNG SHOWING ASBESTOSIS WITH CARCINOMA OF THE LOWER LOBE

vesicular over the greater portion of both lungs, but bronchovesicular in the bases. Fine râles were heard in both apices anteriorly and in the lower right base posteriorly. Coarse râles were audible in both bases posteriorly and over the lower left side anteriorly. The hemoglobin was 68 per cent (Dare). Neither tubercle bacilli nor asbestos bodies were found in several examinations of sputum.

The next admission to the hospital was eight months later. Although the patient had not returned to work, all of his previous complaints had recurred with increased severity. The chest pain was worse on the right. Chest expansion was slight on both sides, and the blood pressure was down to 108 systolic and 68 diastolic. Physical findings in the chest

were at
showed
in the l
priate ti
Aft
to weight
At
had not



FIG 2. SQ

was limited
and cyanot
There
firm as to
mediastinum

Both v
sity, reachi
there were
thick scatte

Section
lower lobe,
part of the
There was
white nodul
usual consis
white nodul
crate emphy
nodule bene
tissue.

ped work
ew years.
rogressive
his pulse
ssure was

alike over
nds were

were about as before, and the finger tips were now clubbed. Sputum examinations again showed no tubercle bacilli or asbestos bodies. Roentgenograms revealed no definite changes in the lung fields as previously noted. A pellagrous skin eruption disappeared under appropriate treatment.

After seventy-seven days in the hospital the patient was again discharged, improved as to weight and general condition, but his dyspnea on exertion did not improve.

At the time of this man's death, sixteen months later, he was not a hospital patient and had not been under close observation for the intervening period. Necropsy (25237-35-33)

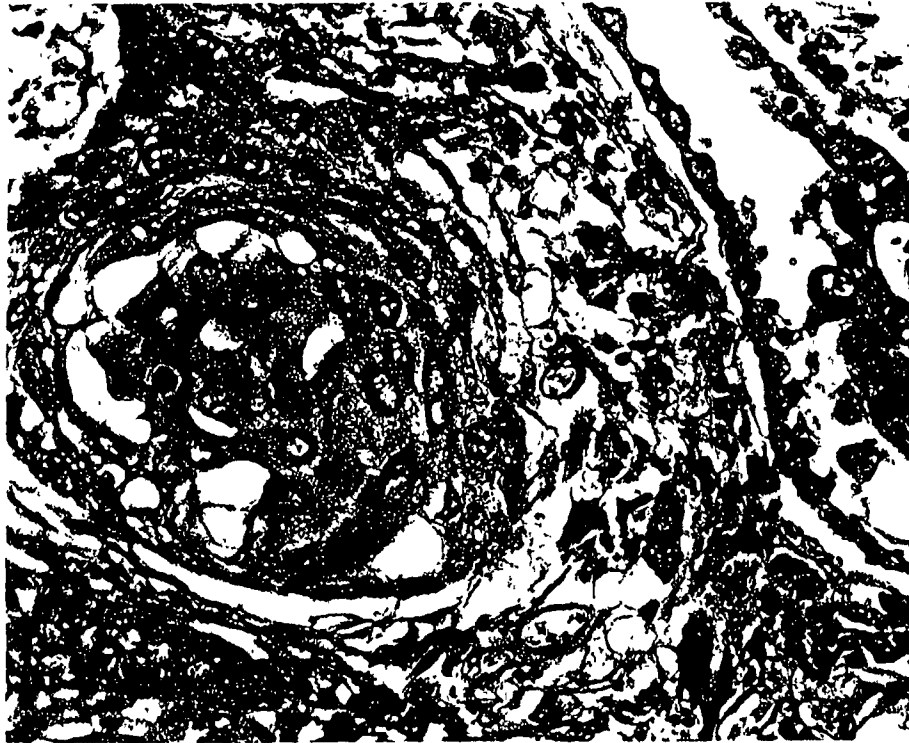


FIG 2. SQUAMOUS-CELL AND GLANDULAR CARCINOMA WITH ASSOCIATED ASBESTOS BODIES $\times 350$

was limited to the chest. The body was greatly emaciated and the finger tips were clubbed and cyanotic.

There was no free fluid in either pleural sac but the pleural surfaces were so thick and firm as to make removal of the lungs difficult. There was a firm dense mass in the upper mediastinum, surrounding the large vessels as they arose from the aorta.

Both visceral and parietal pleurae were thick, nodular, and almost cartilaginous in density, reaching a thickness of 1 cm. over the left lung posteriorly and laterally. In addition there were a number of discrete white firm nodules, 1 to 2 cm. in diameter and about 0.5 cm. thick scattered over both lungs.

Section of the right lung revealed a dense consolidated area in the upper part of the lower lobe, with less complete solidification of the lower part of this lobe. In the axillary part of the lobe a firm, fleshy, cone-shaped mass based on the pleura extended to the hilus. There was marked fibrosis about the bronchi in this region with some stenosis. Several firm white nodules were present in the hilar nodes here, while other nodes were black and of the usual consistency. The lower part of the lobe contained numerous coalescent but separate white nodules. The upper lobe was soft and crepitant, showing nothing more than a moderate emphysema beneath the pleura. In the left lung there was a single circumscribed nodule beneath the pleura in the axillary region, with slight infiltration of the adjacent lung tissue.

ases Fine
y Coarse
orly The
were found

patient had
ed severity.
es, and the
the chest

No lesions of the inner parts of the trachea or large bronchi were found, although there was considerable dense white infiltration about them, especially in the upper mediastinum. This infiltration surrounded the upper portion of the aorta also. The right side of the heart was moderately dilated.

Dense cartilaginous white tissue infiltrated the entire upper mediastinum, holding all structures there rigidly, and extended into the neck as far as could be reached. This was continuous with the thickening of the mediastinal pleura and with the thickening about the bronchi on the right. It was densely adherent to the vertebrae and had to be cut away.

Sections from the right lower lobe, the lower part of the upper left lobe, the pleural nodules, and the mediastinal mass and nodes reveal advanced malignant neoplastic disease, composed in the main of infiltrating masses and cords of stratified squamous epithelium, the cells of which vary in their differentiation from young forms with little squamous cell pro-

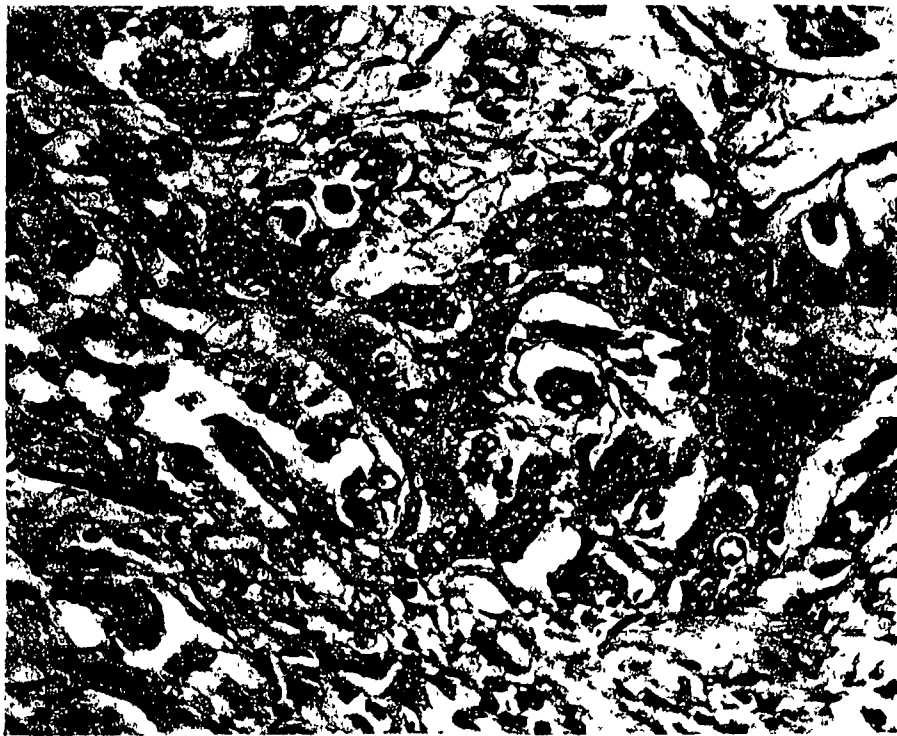


FIG. 3. INFILTRATION OF SQUAMOUS CARCINOMA IN FIBROUS TISSUE WITH ASBESTOS BODIES $\times 350$

duction in the looser tissues to large many-layered masses with polygonal and squamous differentiation and keratinous pearly body production in the denser tissues, such as the pleural nodules. No definite focus of origin can be positively determined, so extensive is the infiltration about bronchi, peribronchial tissues, pulmonary parenchyma, and in the several aspects of the pleura. Within the walls of several bronchi, intermingled with mucous glands, but not upon the mucosa so far as this was examined, the carcinomatous process is actively infiltrating. It permeates the lymph channels widely, infiltrates peribronchial lymph nodes, and has produced dense infiltration about the respiratory tubes and great vessels of the upper mediastinum. It has invaded the walls of the large veins within the lungs and seems actually to have penetrated to the lining.

In certain places, notably in some of the pleural extensions and in the large mediastinal growth, the cancer structures are not epidermoid in form but tubular, with a lining of cuboidal or columnar epithelium, like that of the bronchioles. These tubular structures are seen occasionally in other cancerous areas.

this
sues
withi

uppe
thick
are r
alveo
the
bronc
them

FIG 4

Ir
of asb
gulfed
Asbest
alveola
within
Along
In
granul
in area
nated l
TI
are dila
circulat

It appears that the primary growth is probably in the lower right lobe and that from this has occurred the wide pulmonary, mediastinal and pleural extension. The pleural tissues are generally quite thick, densely fibrous and hyaline. No asbestos products occur within the pleural tissues proper.

Diffusely but irregularly throughout both lungs, more marked in the lower than in the upper lobes, is a widespread old but still progressive fibrosis, increasing the framework and thickening the walls of bronchioles and many alveoli, although in some areas these walls are not thickened and the alveoli are emphysematous. In consequence of fibrosis many alveoli are deformed, some are narrowed, some are distended, and the epithelial lining of the more abnormal is cuboidal, like that of bronchioles. In the more fibrous areas the bronchi and bronchioles are also quite dilated and these, together with the alveoli about them, contain purulent or fibrinous inflammatory exudate.

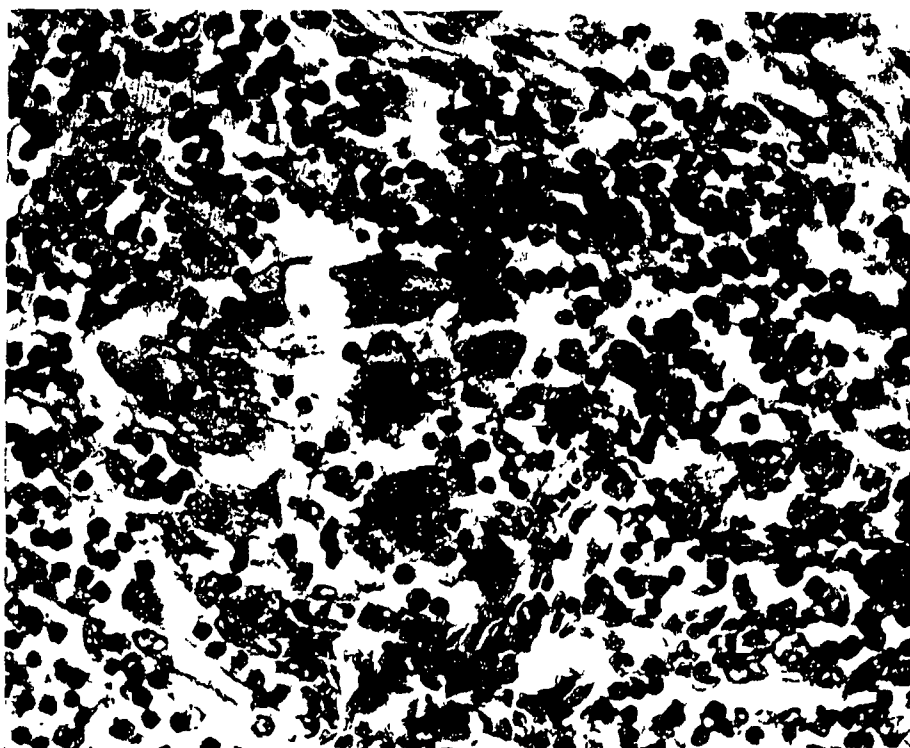


FIG. 4 PERIBRONCHIAL LYMPH NODE WITH DEPOSIT OF ASBESTOS BODIES AND GRANULAR MATERIAL IN LARGE PHAGOCYTES $\times 500$

In many of the air sacs, especially those of the more fibrous areas, there is a scattering of asbestos bodies, singly or in groups, of various shapes and sizes. These are usually engulfed by large multinucleated cells or associated with mononuclear phagocytic collections. Asbestos bodies are also to be found, singly or in small groups, within the fibrosed areas of alveolar walls or peribronchial and perivascular lymph courses. Here they are usually free within the fibrous tissue, although prone to be associated with young connective-tissue cells. Along with these bodies in all locations occur collections of black granular material.

In the peribronchial lymph follicles and hilar lymph nodes are heavy deposits of black granular substance and smaller asbestos bodies and yellowish granular substance, occurring in areas heavily fibrosed, with old hyaline tissue and some young cells. Here are also laminated hyaline nodules, with a fine granular deposit, like the formation found in silicosis.

Throughout the pleural, pulmonary, and mediastinal area, the lymph spaces and vessels are dilated, as if there were considerable obstruction (by carcinoma and fibrosis) to lymphatic circulation.

gh there
astinum.
he heart

lding all
This was
about the
way.
e pleural
c disease,
lum, the
cell pro-



IES $\times 350$

d squamous
such as the
extensive is
in the sev-
with mucous
ous process
eribronchial
s and great
s within the

mediastinal
a lining of
tructures are

In summary, the limited necropsy showed carcinoma of lungs, pleura, and mediastinum, mixed squamous-cell and glandular in form but squamous in the main, judged to be of bronchial origin, pulmonary asbestosis with fibrosis, bronchiectasis, purulent bronchitis and acute bronchopneumonia, dilatation of the right heart

The exposure to asbestos dust in this case was of about twelve to thirteen years' duration, more or less continuous, beginning about fifteen years before death, which occurred at fifty years. There is no means of estimating accurately the duration of the carcinoma, but it was probably making itself felt with the aggravation of symptoms, particularly pain, about two years before death.

It is worthy of note that, although the fibrosis was advanced, it was of the diffuse form generally reported in asbestosis and showed no evidence of the nodular type seen in true silicosis which we have encountered in other advanced cases of asbestosis. The only hyaline nodules found were in the lymph nodes, and these may have been fibrous tubercles.

EPITHELIAL METAPLASIA

It has been interesting to note that in several cases of advanced asbestosis squamous metaplasia of bronchial epithelium has occurred. The following case is summarized in order to record this observation:

A Negro man (No 25145-35-28), who suffered an illness diagnosed as asthma and apparently died from right heart failure, was found at necropsy to have hypertrophy and dilatation of the right heart, minor atherosclerosis of the pulmonary artery, pulmonary asbestosis, chronic bronchitis and bronchiectasis, and acute lobular pneumonia

His lungs were quite voluminous. They did not show the grossly exaggerated fibrous state seen in other cases of advanced asbestosis but in sections fibrosis was observed along the course of interlobular lymphatic distribution. This was mainly an old condition and throughout the fibrous areas were numerous asbestos bodies. In part the fibrosis was disposed in hyaline laminated nodules, such as occur in silicosis, with asbestos bodies embedded within them.

To this silicosis-like nodular fibrosis in asbestosis we have previously applied the term asbesto-silicosis. At the present time we have not determined the significance of this combination type of fibrosis, whether from asbestos dust inhalation entirely or from exposure to other silica dust in addition to asbestos. It has, however, been a conspicuous finding in our material from a number of necropsied asbestosis cases, as previously mentioned.

Asbestos bodies were also found in open alveoli, free and engulfed by macrophages, and in peribronchial lymph nodes. While black granular particles were present in the same areas as the asbestos bodies, they did not appear as the material of true silicosis.

Bronchi and bronchioles throughout showed dilatation, vascular engorgement, mononuclear leukocytosis, denuded lining surface and foci of transformation of undenuded epithelium into stratified squamous form.

The exposure of this man to asbestos dust was not known, but he had told a friend that he had worked in an asbestos plant as a young man and had developed a cough there.

COMMENT

During the past twelve years in 2343 consecutive necropsies we have encountered 7 cases of primary lung carcinoma, including one instance of early occurrence discovered only on histologic examination and the two asbestosis cases. Among these necropsies are 35 showing some degree of asbestosis. In

the m:
few th
In
pulmo
Omitti
in asbe
An
is appi
especie
asbesto
It
vanced
counte
squamo

- 1 LYNCH
2. GLOY
- 3 GLOY
- 4 EGBER
5. NORD
- 6 ANDEI
- 7 VORW
- 8 KLOTZ

the majority this is a minor finding and not the cause of illness or death; in a few the condition is advanced.

Including all necropsies and all lung cancer cases, the incidence of primary pulmonary carcinoma in our necropsy service over this period is 0.3 per cent. Omitting the 35 cases showing asbestos deposits and the 2 cases of lung cancer in asbestosis, the incidence rate is 0.21 per cent.

Among the asbestosis cases (35) the incidence of lung carcinoma (2 cases) is approximately 6 per cent. Whether this is to be taken as of significance, especially in comparison to the general rate, is questionable. The series of asbestosis cases is small and the possible statistical error great.

It has seemed desirable, in addition, to record the observation that advanced asbestosis may lead to bronchial epithelial metaplasia of a type encountered in other locations where cylindrical epithelium may give rise to squamous-cell carcinoma.

REFERENCES

- 1 LYNCH, K M, AND SMITH, W A.: Am J Cancer 24 56, 1935.
- 2 GLOYNE, S Tubercle 17 5, 1935
3. GLOYNE, S.: Tubercle 18 100, 1936.
- 4 EGBERT, D. S, AND GEIGER, A. J.. Am. Rev. Tuberc. 34 143, 1936.
- 5 NORDMANN, M Ztschr f Krebsforsch 47 288, 1938.
- 6 ANDERSON, C S, AND DIBLE, J H J Hygiene 38. 185, 1938.
- 7 VORWALD, A. J, AND KARR, J W Am J. Path 14 49, 1938
- 8 KLOTZ, M. O.: Am. J Cancer 35 38, 1939