THE ASSOCIATION OF SILICOSIS AND CARCINOMA OF THE LUNG

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With the exception of the pulmonary tumours occurring among the miners at Schneeberg and Joachimstal and described by Rostoski, Saupe and Schmorl (1) and by Pirchan and Sikl (2), the rapidly accumulating literature on lung cancer has contained only isolated reports of carcinoma of the lung occurring in association with the various forms of pneumoconiosis. Since both these lesions are being recognized with greater frequency, it may be expected that reports of the coexistence of the two will be increasing. As yet, however, the number of recorded cases of primary lung cancers associated with pneumoconiosis is too small to determine conclusively whether the two conditions are in some way related or whether their association is purely accidental. The data to be presented in this paper indicate that silicosis may be a definite predisposing factor in the development of carcinoma of the lung.

The tumours of Schneeberg and Joachimstal will not be considered here because the radioactivity of the dust as well as that of the inhaled air confuses the picture. That this radioactivity is probably of prime import in these cases is suggested by the fact that it is a factor common to both mines (2). Apart from these cases a great variety of irritating atmospheric conditions and inhaled dusts have been mentioned as possibly predisposing to lung tumours but in only a few instances has it been possible to establish such a relationship. Investigations of the occupational incidence of pulmonary neoplasms have been of little help. Hruby and Sweany (3) found labourers, office workers, and housewives to be most frequently affected, while representatives of other vocations were affected in proportion to their numbers. Analysis of death certificates (which is open to criticism) for England and Wales made by Kennaway and Kennaway (4) indicated that the factors leading to silicosis were not active in predisposing to lung cancer. These investigators, did, however, find that the highest incidence of the latter disease occurred among open-air workers exposed to road dusts, with the exception of motor vehicle operators. It is worthy of note that no increased incidence was found among cotton-mule spinners, though these workers inhale oils generally believed capable of producing skin cancers. Twenty of 41 patients suffering from pulmonary neoplastic disease, reported by Frommel (5), were found to have been exposed to various dusts. Rosedale and McKay (6), in reviewing 57 cases of carcinoma of the lung were struck by the fact that 75 per cent of the patients had been employed in occupations requiring exposure to dusts or other irritating atmospheric conditions. Advanced pneumoconiosis was found in 14 of their cases, some of which showed marked fibrotic changes. As pointed out by Boyd (7), however, it is questionable if air contaminated by automobile fumes or material from tarred roads is of any importance, as he found a high inci-
idence of lung tumours in Winnipeg, Manitoba, in patients coming from regions where these factors could not possibly have played a part.

Those who have reported cases of primary lung tumour associated with some form of pneumoconiosis vary in their opinion of the relationship between the two diseases. Considerable caution must be exercised in evaluating the data bearing on this aspect. Analysis of radiological statistics alone is likely to be misleading, inasmuch as pulmonary neoplasms are frequently difficult to demonstrate by x-rays. Indeed, in the cases to be presented here a diagnosis by this means could be made in not a single instance, even in retrospect. Radiologic evidence of pneumoconiosis, if present, is usually not to be disputed, although it is often difficult to designate the type. Furthermore, as several cases of the present series show, the pneumoconiosis may be so slight that diagnosis is assured only post mortem and still there may be an associated tumour. Harris (8) has pointed out that occasionally massive hilar lesions in pneumoconiosis may simulate tumour. Post-mortem examinations should include, in addition to the gross study, a careful microscopic examination of tumour-free lung by one familiar with the changes compatible with a pneumoconiosis, as otherwise any fibrosing process encountered may readily be overlooked, particularly if slight, or may be misinterpreted as a response to the presence of the growth.

In a recent review of the subject based on a large series of radiologic and post-mortem reports collected from their own material and from the literature, Vorwald and Karr (9) concluded that the incidence of carcinoma of the lungs is not increased among those suffering from pneumoconiosis, but is, if anything, actually decreased. These workers mention in their review a case of bronchogenic carcinoma occurring in a haematite miner, reported by Stewart and Faulds (10). This case cannot be considered as one of tumour associated with pneumoconiosis, as the lungs were originally described as normal apart from the growth and some emphysema. Also referred to in this report are 3 cases of carcinoma of the larynx associated with pneumoconiosis, described in a roentgenologic report by Harris (11).

Oskar Klotz (12) first reported in detail a case of carcinoma of the lung and silicosis (which is briefly summarized in this paper) and concluded that "the observations on the occurrence of cancer of the lung in relation to silicosis are too few to allow any general statement to be made in this regard." Pancoast and Pendergrass (13), who reported two cases of bronchogenic carcinoma, proved by biopsy, associated with moderate pneumoconiosis as demonstrated radiologically, do not believe that the pneumoconiosis predisposed to the neoplastic process. Their opinion is based on their extensive radiological experience, in which the coexistence of these lesions had been encountered with extreme rarity. Allen (14), who was able to confirm the clinical diagnosis in one of the above cases by autopsy and who also reported the post-mortem findings in a case of his own, supports this negative view and suggests that "the incidence of primary lung malignancy is probably no higher among workers exposed to silica dust than it is among the general population at large." In only 2 of 69 cases of bronchogenic carcinoma did Olson (15) find pneumoconiosis, and this with only moderate fibrosis. In these cases it was believed that the part played by the pneumoconiosis was insignificant.
Dible (16) found 4 instances of malignant growth in autopsies on 14 silicosis subjects. Two had primary lung tumours, and in one of these there was a second primary cancer arising from the colon. Dible believed that a connection between malignant disease and silicosis was indicated in the cases of pulmonary cancer, while the existence of multiple malignancy in one case is compatible with the view of a diffusible carcinogenic agent. Fine and Jasso (17), who report one case of primary bronchogenic carcinoma found in autopsies on 22 silicotics, are of the opinion that the combination of the two diseases is not uncommon, but that it is rarely seen because so few cases of silicosis come to autopsy.

Lynch and Smith (18), in reviewing a case of asbestosis in which there was an epidermoid cancer probably arising from a bronchus showing squamous metaplasia, suggest that "a conception of its origin by reason of chronic bronchial irritation is compatible with the current view of the etiology of such tumours." Likewise Egbert and Geiger (19) in referring to their case of primary lung cancer in asbestosis suggest that the inhalation of the irritating asbestos may have played a part in the development of the tumour. Gloyne (20, 21), who has reported two cases of squamous-cell and one of oat-cell cancer in lungs showing asbestosis, also inclines to the belief that there may be some relationship.

In addition to these cases, Sladden (22) tabulated two cases of bronchogenic carcinoma occurring in 60 cases of silicosis, but owing to the character of the paper made no comment regarding the coexistence of the conditions. In one of these cases the fibrosis was slight while the silica content of the dried lung was 0.10 per cent. In the second case the fibrosis was designated as "much" while the silica content of dried lung was 1.02 per cent.

Middleton (23) in a review pertaining largely to silicosis refers to 3 cases of lung cancer in 54 cases of asbestosis. Maxwell (24) describes another case of carcinoma and silicosis, where the diagnosis was based on radiological findings and a suspicious biopsy. A case of primary carcinoma associated with anthracosis (silica content of lungs normal) is recorded by Sweany (25) in a comprehensive study of 40 cases of pneumoconiosis.

It is difficult to evaluate these findings and to determine their actual significance. Though the coexistence of the conditions has been observed with amazing infrequency by some, others feel that this may be due to the lack of suitable material. In the main the tendency is to support the contention that silicosis or other forms of pneumoconiosis may play a part in the production of primary carcinoma of the lung.

The following review is based upon 50 cases of silicosis observed from 1925 to 1936 inclusive in the Department of Pathology and Bacteriology of the University of Toronto. Twenty-five of these are from the autopsy files of the department while in 25 the material was submitted by the Department of Health of Ontario for examination. Among these 50 cases, 9 instances of carcinoma were found, including all organs. This is an incidence of only 18 per cent, which is not significantly different from the incidence in a larger unselected group (Table I). This figure may possibly be too low, as the material submitted by the Department of Health consisted in most cases of the thoracic organs only and primary growths elsewhere in the body could not be
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Table I: Comparison of the Incidence of Primary Carcinoma of the Lung in Silicosis and in Unselected Cases

<table>
<thead>
<tr>
<th></th>
<th>Total Number of Cases</th>
<th>Cases of Carcinoma (all organs)</th>
<th>Carcinoma of the Lung</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Percentage of total</td>
<td>Number</td>
</tr>
<tr>
<td>Cases of silicosis</td>
<td>50</td>
<td>9</td>
<td>18.0%</td>
</tr>
<tr>
<td>Unselected cases</td>
<td>4500</td>
<td>808</td>
<td>17.7%</td>
</tr>
</tbody>
</table>

excluded. Of the 9 tumours, 4 were primarily bronchogenic, which is 8 per cent of the total number of cases of silicosis and 45 per cent of all the cancers found in this group.

For the sake of contrast these observations may be compared with a group of 4,500 autopsies performed in this department between 1925 and 1936 inclusive. These autopsies were carried out on patients dying in the Toronto General Hospital, which has active services in all departments except pediatrics and infectious diseases. The hospital population is composed largely of urban dwellers and to a lesser extent is fed from rural communities, so that it is not a true cross-section of the population as a whole. In this series of cases, 808 carcinomas of all organs, or 17.7 per cent, were found. Of these, 53 were primarily bronchogenic, which is 1.17 per cent of all autopsies or 6.5 per cent of all cancers. Both these figures are considerably lower than those of the first group. The lung was the third most common site in which cancerous growths were encountered at autopsy, being preceded only by the large bowel (including the rectum) and the stomach.

The average age incidence of those showing primary lung cancers in this larger series was fifty-two years and nearly all were labourers of one kind or another. Nine had given their occupation as miners, 3 as metal workers and 2 each as labourers, gardeners, gas company employees, engineers, and laundry men. Among those describing themselves as miners, only one showed evidence of silicosis (Case 4). Fourteen, or 26.29 per cent, can be considered to have pursued occupations necessitating the inhalation of air containing either dust or other foreign matter.

Though it is not entirely accurate to compare a selected group of 50 cases with a control group numbering 4500, a comparison of the figures suggests that the incidence of carcinoma of the lung in silicotics may greatly exceed that among the population at large. The findings have been summarized in Table I.

Case Reports

The four cases in which silicosis and carcinoma of the lung were coexistent are here presented in detail.

Case 1 (P-98, previously reported by Klotz, 12): A fifty-year-old man, besides having been employed in the nickel mines of Sudbury, Ontario, had worked in a granite quarry for five years. His complaints were dyspnoea and cough of three weeks' duration, watery spu-
tum, substernal pain, weakness, and loss of weight. X-ray films showed evidence of pneumoconiosis and also of fluid on the right side. Above the fluid was an area of marked density with a ragged outline, its base towards the mediastinum. Sputum was negative for tubercle bacilli; the aspirated fluid contained only red blood cells. Other findings were essentially negative. Clinically, the presence of a new growth was suspected.

**Autopsy:** The pathological specimen consisted of the thoracic viscera only. The pleural surfaces of the lungs were of a bluish-black colour with small, firm, greyish nodules, the size of a pea, and massive fibrous adhesions on the right. The cut surfaces of the lungs were studded with numerous small, firm, discrete, black nodules which for the most part were smaller than a pea. The right lung showed much pigmentation. A large tumour surrounded and partially occluded the right main bronchus at the point of its secondary divi-

![Image](https://via.placeholder.com/150)

**Fig. 1. Case 1: Primary Carcinoma and Silicosis of the Lung**

sions (Fig. 1). This was pinkish-white in colour, firm about the bronchi but more friable in its distal portions. The tumour itself occupied the lower half of the right upper lobe and spread from the hilus towards the periphery. Tumour nodules were also seen following the course of the blood vessels and bronchi, and metastatic masses were found amid the pleural adhesions of the right lung, at the apex of the left lung, in the peribronchial and hilar nodes on both sides, and in the mediastinal lymph nodes and tissues. The aorta and pulmonary artery were embedded in this latter massive growth. Owing to the limited examination the presence of distant metastases could not be determined.

**Microscopic Examination:** Sections from representative areas were studied. Scattered throughout the parenchyma of both lungs were numerous fibrous nodules containing the fine granular and doubly refractile crystals of silica. These nodules varied greatly in size. Frequently they consisted of small irregular masses of connective tissue along blood vessels and bronchioles, while at other times they were distinct laminated hyaline fibrous lesions in which only small, diffuse deposits of silica were evident. They were most numerous to-
wards the hilar regions and were also encountered in the lymph nodes. This aspect of the microscopic picture was typical of a moderately advanced silicotic process. Sections of the areas involved by tumour showed all the parenchyma lying between the fibrous nodules to be replaced by a malignant neoplastic growth. The cells constituting the tumour were, for the most part, small, spindle-shaped, closely compacted, possessing little cytoplasm, and to some extent having a sarcomatous appearance. Mitotic figures were numerous. In small clefts and lymphatic channels the tumour assumed a pseudo-alveolar and glandular character. The extension of the growth into new portions of the lung did not appear to have any direct relationship to the fibrotic nodules. It was noted, however, that where fibroses were present the tumour grew with greater activity on the peripheral borders and sometimes invaded the nodule itself (Fig. 2). Extension had occurred not only by way of the lymphatics and interstices but also via the air sacs and bronchioles, which in many areas were filled with the malignant cells. Further study of the material from this case has revealed marked metaplastic change in the tracheal mucosa to a stratified squamous type. This was evident at a point where the trachea was surrounded, compressed, and at some points invaded by the growth. No metaplasia could be found in the sections of the peripheral bronchi.

Analysis of the lungs showed 33.98 per cent of the dry ash to be composed of silica dioxide.\footnote{Silica estimations in this and the following cases were carried out by Dr. C. M. Jephcott, Division of Industrial Hygiene, Department of Health of Ontario, to whom I am deeply indebted for this work.}

CASE 2 (P-132): A forty-five-year-old man had worked for fifteen years in English tin mines and for nine years in the gold mines of Northern Ontario. He was first examined two years before death, at which time he was complaining of slight morning cough, but no abnormal findings were encountered. X-ray films of the lungs showed some increase in the general linear markings with a suggestion of mottling and a soft shadow running into the aorta on the left. One year after these plates were taken, routine re-examination showed a cluster of medium-sized areas of soft-looking density in the upper horn of the left hilus. Death occurred eighteen months later, at which time the patient was complaining of cough.
dyspnoea, and weight loss. X-ray study shortly before death revealed shifting of the heart and mediastinum to the left, with a soft homogeneous shadow from the apex to the 6th rib on the left. Coarse, fluffy mottling was present below this.

**Autopsy:** The gross material consisted of the lungs, heart, and mediastinal structures. The heart was essentially normal in all respects. The pleura of both lungs was deeply pigmented but not appreciably thickened. The cut surfaces showed a heavy mottling with fine blackish areas which lay in relation to small blood vessels and bronchi and were, for the most part, impalpable; a few of them, however, could be felt. A large, firm, whitish, coarsely lobular mass measuring $12 \times 6 \times 6$ cm. occupied the central portion of the left lung (Fig. 3). This tumour possessed several outlying nodules and was continuous with the massively involved peribronchial, hilar, and mediastinal lymph nodes. Its bronchial relationships could not be determined. The lung tissue of the base and apex of this lung showed a greyish consolidation which appeared to be partially due to diffuse extension of the tumour growth and partially inflammatory. The bronchi in the outlying areas distal to the mass were plugged with a gelatinous coagulum. A huge mass of tumour the size of a baby's head lay in the mediastinum. This was composed of agminated lymph nodes, the outlines of which could still be identified. These nodes contained considerable pigment, but there was none in the tumour tissue between them. The right lung was entirely free from neoplastic change. The presence of distant metastases could not be determined because of the limited material available for study.

**Microscopic Examination:** Sections from representative areas of the lungs showed tumour, tuberculous caseation, and dust nodules. In the uninvolved portions, the alveolar walls were slightly thickened, dilated, and in many places ruptured, producing an emphysematous condition. The silicotic lesions were small, though some appeared sufficiently large to be palpable. These consisted of perivascular and peribronchial masses of laminated collagenous connective tissue containing much doubly refractile dust. The perivascular sheaths were diffusely thickened by the fibrosing process. The areas of caseation were from the consolidated regions of the left lung. The caseous process was widespread; it was essentially intra-alveolar and had called forth little cellular reaction, though here and there typical tubercles were to be found in the outlying tissues. The silicotic lesions in these areas were obscured by the caseous process.

The tumour was composed of moderately large spindle-shaped cells with round or ovoid nuclei which stained less deeply than is usual in oat-cell tumours. All the variations characteristic of malignancy were demonstrated by the growth, while mitotic figures were fairly numerous. The cells grew in compact masses which here and there showed a feeble tendency to palisading while elsewhere the arrangement slightly resembled an epidermoid carcinoma. The supporting stroma was delicate and not unduly vascular. Extension of the growth had occurred along the lymphatics and interstices, destroying all the pre-existing pulmonary elements and compressing the adjacent structures. No growth was demonstrable within the airways proper. No relationship appeared to exist between these various processes and no metaplasia of the bronchial epithelium was found in any of the sections.

Though the fibrosing process was not extreme, analysis revealed the following percentages of SiO$_2$ in the dry ash of the lungs: left, 21.64 per cent; right, 26.94 per cent.

**Case 3 (P:173):** A forty-five-year-old man had worked in English tin mines for fifteen years and later in various hard rock gold mines of Northern Ontario for a total period of approximately fifteen years. He was removed from underground work ten years before his death and subsequently occupied his time as a prospector and at various jobs above ground. Four years before death he was suffering from a slight cough with scanty sputum, dyspnoea, and vague substernal distress. Radiologically the condition was considered as a border-line case of silicosis and compensation was refused because of the indefinite character of the pulmonary condition. The patient was again examined nine months before death and still showed only a pre-silicotic degree of fibrosis. Two months before death he developed an acute respiratory condition. He died in the hospital, where large quantities of blood-stained fluid were aspirated from his left pleural cavity. A clinical diagnosis was not made.

**Autopsy:** The gross specimen consisted of both lungs, heart, and mediastinal structures intact. The heart revealed no significant lesion. Scattered throughout the intact parenchyma of both lungs were numerous small, palpable, firm, slightly gritty and deeply pig-
mented masses measuring up to 1 to 2 mm. in diameter. These were discrete and occurred largely in relationship to the peribronchial and perivascular regions. The middle and lower lobe of the right lung was consolidated by a uniform pneumonic process, while the overlying pleura was coated with fibrin. The left lung, which was covered by ragged, fibrotic pleura was largely replaced by tumour tissue, air-containing parenchyma being present only at the apex. This growth proved to have arisen from a large mass about the main bronchus, occupying the submucosa and greatly narrowing this structure without gross evidence of ulceration (Fig. 4). The tumour had extended out, freely infiltrating the lung and forming a thick, subpleural layer over the anterior and inferior aspects. The growth was composed of firm, uniformly greyish-white, non-pigmented tissue. This mass was continuous, via the involved peribronchial and peritracheal nodes, with that in the medastinum which surrounded the great vessels and aæophagus. This was composed of invaded lymph nodes which could still be outlined by their pigmented periphery.

Again the limited material made the determination of distant metastases impossible. 

Microscopic Examination: Microscopically the more normal portions of the lung showed air-containing tissue with numerous dust-laden phagocytes. The perivascular lymphatics were surrounded by collagenous, fibrous tissue which was in excess of that ordinarily found with the degree of anthracosis present. Examination of these nodules by polarized light showed scattered silicotic crystals. No nodules were found at any distance from vessels or bronchi. Sections from the areas of inflammatory consolidation were typical of an acute lobar pneumonia. The tumour was found to be composed of very small cells with
scanty cytoplasm, which was scarcely visible, and round or ovoid, deeply staining nuclei. The cells were haphazard in arrangement, forming solid masses and sheets which were supported by a delicate stroma of fibrous connective tissue. In some areas the stroma consisted of much denser strands of connective tissue bearing no resemblance to the pre-existing lung but showing at wide intervals collections of pigment similar to those seen in the silicotic lesions. The tumour cells spread freely through the tissues, infiltrating the alveolar walls and perivascular lymphatics rather than spreading through the air spaces. Dark dust cells were numerous in the alveoli around the advancing margin of the tumour. Sections from the main bronchus failed to prove the point of origin of the growth. Here the intact ciliated epithelium passed freely over masses of tumour cells which had widely separated it from the cartilaginous rings and was infiltrating between the mucous glands.

![Fig. 4. Case 3: Primary Carcinoma and Silicosis of the Lung](image)

The lung has been cut from the hilum outwards and the two halves spread apart. The main bronchi, which are occluded by tumour, have been split so that half appears on each surface.

FIG. 4. Case 3: Primary Carcinoma and Silicosis of the Lung

Thus these lungs demonstrated a minimal degree of nodular fibrosis associated with a carcinomatous process. Ashing of the tumour-free right lung revealed only 14.3 per cent of the ash to be composed of $\text{SiO}_2$.

**Case 4 (A-230-36)** This patient, a fifty-four-year-old man, had been a gold miner for twenty-three years. He was admitted to the hospital with a thirteen-month history of lumbar pain which later spread to involve hips, thighs, and knee-joints, and finally the left arm. He also complained of a chronic cough and dyspnoea of two and a half years' duration. Chest plates were suggestive of a basal tuberculous lesion, but sputum examinations were negative. A final clinical diagnosis of Marie-Strümpell arthritis and silicosis of the lungs was made.

**Autopsy:** At autopsy a small primary tumour was found at the hilus of the left lung, arising from the left main bronchus and producing some stenosis of this bronchus and partial occlusion of the left pulmonary artery. On section of the mass it presented a yellowish-grey, carcinomatous appearance and was extremely firm in consistency. In addition, throughout
all parts of both lungs small, shotty, hard, black nodules the size of millet seeds could be palpated. This primary tumour had given rise to secondaries in the vertebral column, pelvic bones, and femur.

Microscopic Examination: The tumour was composed of atypical polyhedral epithelial cells growing in strands and masses and showing numerous mitotic figures. In some areas the cells tended to arrange themselves in epidermoid sheets, while elsewhere a pseudo-gland-like formation was noted. Several small clusters were composed of definitely spindle-shaped cells. The supporting stroma was extremely dense and was extensively infiltrated by chronic inflammatory cells. The silicotic lesions were represented by the extensive fibrous tissue scarring in the regions not involved by tumour. This was most marked in the subpleural and peribronchial areas, where the fibrotic nodules were bordered by large numbers of phagocytic cells heavily laden with dust pigment, much of which proved to be doubly refractile. In other sections these cells could be found plugging lymphatics and associated with a definite fibrous tissue proliferation forming small hyaline nodules without any inflammatory reaction. This nodular fibrosis was interpreted as an early response to an inhaled irritant, presumably silica. Mineralogical estimations on the lungs were not carried out.

Table II briefly summarizes some of the significant facts pertaining to the above cases.

**Table II: Summary of Cases of Silicosis and Cancer of the Lung**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Exposure to SiO₂</th>
<th>Duration of Symptoms</th>
<th>SiO₂ Content of Lungs</th>
<th>Fibrosis</th>
<th>Site of Tumour</th>
<th>Type of Tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>5 years+</td>
<td>3 weeks</td>
<td>33.98%</td>
<td>++</td>
<td>Right hilus</td>
<td>Anaplastic</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
<td>24 years</td>
<td>2 years</td>
<td>21.64%</td>
<td>+</td>
<td>Left hilus</td>
<td>Anaplastic</td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>30 years</td>
<td>4 years</td>
<td>14.3%</td>
<td>Minimal</td>
<td>Left hilus</td>
<td>Anaplastic</td>
</tr>
<tr>
<td>4</td>
<td>54</td>
<td>23 years</td>
<td>2½ years</td>
<td>-</td>
<td>Minimal</td>
<td>Left hilus</td>
<td>Epidermoid (scirrhous)</td>
</tr>
<tr>
<td>Average</td>
<td>48</td>
<td>20.5 years</td>
<td>25.5 months</td>
<td>23.3%</td>
<td></td>
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</tr>
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**DISCUSSION**

The symptomatology exhibited by these patients was not atypical for carcinoma of the lung. Dyspnoea, cough, substernal pain, haemoptysis and loss of weight and strength were the prominent complaints. The duration of symptoms varied from three weeks to four years with an average of twenty-five months. In Case 4 the respiratory complaints were masked by those produced by metastatic destruction of various bony structures. In 2 cases (1 and 3) bloody pleural fluid was obtained on thoracocentesis. In no instance was a radiological diagnosis made, though all the patients had been subjected to x-ray examination.

The average age of these patients was forty-eight years and with one exception (Case 1) all had been exposed to silica for a period exceeding twenty years (Table II). This last figure does not differ materially from that often given as the average duration of exposure in cases of pure silicosis. It is worthy of note in this connection that in Case 1, although the known exposure was only five years, yet the lungs showed the most advanced degree of fibrosis
and on analysis yielded the highest percentage of silica (33.98 per cent). The remaining cases showed only a minimal or slight degree of fibrosis attributable to the siliceous deposits. Case 2 alone presented evidence of tuberculosis and here the infective process had taken the form of a tuberulous bronchopneumonia.

All the tumours were hilar in position, arising from the main bronchi on the left in three cases and on the right in one (Table II). Microscopically there was a great similarity between the growths observed in Cases 1, 2 and 3, which were of the spindle-cell or oat-cell anaplastic type, though, as is usual in such neoplasms, it was frequently possible to find islands of cells tending towards a more highly differentiated form. Case 4 showed a poor differentiation towards the epidermoid type. With the exception of Case I, where some increased growth of the tumour was noted in the regions bordering the silicotic lesions, no anatomical relationship was demonstrable between the neoplastic changes and the fibrosing process. All cases, however, did show deposits of pigment-containing cells in lymphatics. Metaplasia of the bronchial epithelium was never observed, though such changes were noted in the tracheal mucosa in one instance.

An analysis of the material available in this department, as shown in Table I, and a study of the literature suggest strongly that the coexistence of carcinoma of the lung and silicosis is not purely accidental, and that individuals suffering from silicosis, even in its early stages, may be more prone to develop a carcinoma of the lung than the remainder of the population not so exposed. Complete confirmation of this suggestion, however, requires the accumulation of further accurate statistical data.

From an anatomical point of view we are forced to admit that the part actually played by the silica is obscure. It is possible that silica itself possesses carcinogenic properties and, acting directly on the bronchial epithelium, stimulates it to neoplastic activity. This would seem unlikely, as no undue incidence of bronchogenic tumours has been reported among laboratory animals exposed to dusting experiments (9, 26). It must be remembered, however, that animals so treated usually survive for a relatively short period of time. On the basis of the same argument we are also led to doubt whether the chronic irritation produced by the silica, either chemical or physical, is of great significance, as it is rarely that precancerous epithelial changes are observed in the bronchi of "dusted" animals (26). If the parenchymal changes resulting from the silica constitute an indirect factor in the production of the growth, a high incidence of lung cancer might well be expected in other chronic fibrosing pulmonary conditions such as bronchiectasis, tuberculosis, interstitial pneumonia, and lung abscess. With the exception of tuberculosis, these lesions when associated with a pulmonary tumour are generally considered to be secondary to chronic bronchial obstruction produced by the growth itself. It may be argued that as yet unrecognized carcinogenic substances are possibly present in the inhaled air. This would seem doubtful since, if such were the case, an increased incidence would exist among all exposed and not only among those showing the effects of silica in the form of silicosis. Thus, in spite of the lack of direct evidence, we are led back to the silica itself as the offending agent.
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Summary

The literature pertaining to the association of silicosis and carcinoma of the lung is briefly reviewed. An analysis of the statistics of the Department of Pathology and Bacteriology, University of Toronto, shows an incidence of lung cancer of 8 per cent among 50 silicotics as compared with an incidence of 1.17 per cent among 4500 unselected cases.

Four cases of carcinoma of the lung associated with silicosis are recorded, and the possible significance of silica in relation to the etiology of cancer of the lung is briefly discussed.

Note: The invaluable assistance rendered by Dr. G. Lyman Duff in the preparation of this paper is gratefully acknowledged.

Bibliography