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# SURVEY OF SOME CURRENT BRITISH AND EUROPEAN STUDIES OF OCCUPATIONAL TUMOR PROBLEMS

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ON JUNE 28, 1950, I sailed from New York with the object of visiting individuals engaged in the study of occupational tumor problems abroad. Experience gained from these visits provides the material of this report and will be presented under the following headings:

I. Shale Oil
II. Petroleum
III. Asbestos
IV. Dyestuffs
V. Sources of Statistical Data on Occupational Factors in Cancer.

## I. SHALE OIL

Skin cancers in paraffin workers in the Scottish shale-oil industry were noted as long ago as 1876. In 1923, a detailed study of this problem with a report of 65 cases was prepared by Dr. Alexander Scott [1] at the request of the Scottish shale-oil industry. Dr. Scott has continued since that time to serve as medical consultant for the industry and as works physician. I had the privilege of visiting him at the Pumpherston Works in Mid-Calder, Scotland, where I also had the pleasure of meeting Mr. Alan Anderson, the works manager, Dr. E. Smith, the chief chemist, and Mr. Crombie, works chemist. Mr. Crombie gave me a tour of the plant. He stated that oil shale, the material taken out of the earth, is retorted at 1000 to 1900 F. at four plants in Scotland to yield naphtha, ammonia, and crude oil. The products are then sent to the Pumpherston Works, where they are processed to yield gasoline, industrial naphthas, paraffin, diesel oil, coke, and acid sludge.[2] The paraffin is obtained by a pressing operation, to be commented on in more detail later.

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Presented at a meeting of the Cancer Prevention Committee in New York, Oct. 18, 1950.

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1. Scott, A.: On the Occupation Cancer of the Paraffin and Oil Workers of the Scottish Shale Oil Industry, British M. J. 2:1108-1109 (Dec. 9) 1922; The Occupation Dermatoses of the Paraffin Workers of the Scottish Shale Oil Industry, with a Description of the Systems Adopted and the Results Obtained at the Periodic Examinations of These Workmen, Eleventh Scientific Report, Imperial Cancer Research Fund, London, 1923, pp. 1-94; Shale Oil Industry in Occupation and Health, Report No. 242, International Labour Office, Geneva, 1925.

2. A Brief Description of the Operations of the Scottish Shale Oil Industry, Scottish Oils Ltd., Glasgow, 1948. (32 pp.)



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He then covered his arm again with the lubricating oil, but this time rubbed it off with cotton soaked in a colorless technical grade of white oil. Almost all the fluorescence was thus removed, only a little remaining in a very few scattered hair follicles. Dr. Cruickshank stated that he had not found dermatitis to result in human skin washed repeatedly with white oil, provided the skin was healthy to start with. Cases of irritation occurred when the oil was applied under dressings. Further discussion of ways to protect the skin against oils is contained in my section on "Shale Oil."

Dr. Cruickshank and Prof. Squire have described warts that occurred on the skin of 33% of a group of 138 machine-tool operators exposed to sprays of a cutting oil which they found capable of inducing skin tumors in animals.[13] I had an opportunity to examine many excellent photographs of these men. Some of the lesions were flat, white keratoses; others were raised, rugose, and pigmented. Histological sections showed the latter to be papillomas. One man had a scrotal cancer, sections of which I saw. Photographs of his arms showed half a dozen small papillomas.

Prof. J. W. Cook, at the University of Glasgow, is attempting to identify the chemical nature of the carcinogens in the petroleum oils under biologic test at Birmingham. Prof. Cook was away from Glasgow when I visited his laboratory, but the work was described to me by his assistant, Dr. W. Carruthers. By high-vacuum distillation, chromatography on alumina, and purification with picric acid, they have isolated a chrysene with a long aliphatic side chain. Their general procedure is to extract the oils with sulfur dioxide, run the extracts through alumina columns, and elute with petroleum benzin. They have thus obtained four crystalline compounds, as yet unidentified, of which two are aromatic. Only one has been obtained in sufficient quantity for biologic test, but results are not yet to hand.

They have failed to find benzpyrene. The method of search was to extract the aromatics with sulfuric acid, regenerate the hydrocarbons, and examine by fluorescence spectroscopy. Dr. I. Hieger, of the Chester Beatty Institute, London, was also said to have searched unsuccessfully for benzpyrene in lube oils found carcinogenic at Birmingham. I may note here that a very simple procedure for the detection of benzpyrene was demonstrated to me by Mr. Robert Waller in Sir Ernest Kennaway's laboratory in London. An account of this method will appear shortly in the *British Journal of Cancer*. All parties agreed that absorption spectroscopy was useless as a means of identifying compounds in complex mixtures, such as oils, and emphasized the need for fluorescence spectroscopy.

### III. Asbestos

The 1947 report of the Chief Inspector of Factories[14] noted the presence of cancer of the lungs or the pleura in 31 (13.2%) of 235 cases of asbestosis recorded in the 23 years from 1924 through 1946. These figures stimulated interest in the question of whether lung cancer is an occupational hazard in the asbestos industry and, if so, which phases of the industry and what working conditions present such a hazard. The data cited above were prepared by the Senior Medical Inspector of Factories, Dr. E. R. A. Merewether, whom I visited.

13. Cruickshank, C. N. D., and Squire, J. R.: Skin Cancer in the Engineering Industry from the Use of Mineral Oil. Brit. J. Indust. Med. 7:1-11, 1950.

14. Annual Report of the Chief Inspector of Factories for the Year 1947. London: His Majesty's Stationery Office, 1948, pp. 79 to 81. Price 3 shillings.

Dr. Merewether referred to the governmental report published in 1930 by himself and C. W. Price.[17a] This report showed that asbestosis developed in 80% of men employed 20 or more years in the industry[17b] and that in various groups of workers the percentage in which asbestosis developed varied directly with the dustiness of the process in which the groups were engaged.[17c] These findings led to the adoption of laws requiring ventilation of asbestos work rooms in Great Britain (Asbestos Industry Regulations, 1931). Detailed specifications for safety equipment are contained in Factory Orders, 1944. It should be noted that there is no mining of asbestos in England. Hence, the British figures refer only to individuals engaged in weaving or other manufacturing or handling operations.

A first problem was whether the apparent association of lung cancer and asbestosis means merely that workmen's compensation procedures funneled all chest diseases into one group. This possibility cannot be supported, however, for no such high incidence of lung cancer has been found in cases of silicosis, which are likewise reported to and reviewed by the Pneumoconiosis Board. Cancer of the lungs or the pleura was noted in only 91 (1.32%) of 6,884 cases of silicosis recorded from 1930 through 1946.[18] The incidence of cancer was thus 10 times greater in asbestotic lungs than in silicotic lungs. Data on the average age at death in this silicotic group were not given, but the same report listed a series of 1,037 silicotics who died at an average age of 58.2 years, compared with a group of 160 asbestotics who died at an average age of 47.5 years. Therefore, the difference in cancer incidence in the two diseases could not be attributed to death of silicotics before they reached the "cancer age"; in fact, the silicotics would appear to have had greater opportunity by a full decade to yield cancers. Similarly, the average duration of employment in these two groups could not account for the difference: 34.3 years for the silicotics against 14.9 years for the asbestotics.

A measure of the rate at which lung cancer occurs in the general population of England and Wales can be found in the Registrar General's Statistical Review (1949). Employing the data given on pages 3 and 145 of the Review, one can calculate that 1.36% of all deaths in the three years from 1943 to 1945 were reported as due to cancer of the lung, the bronchus, or the pleura. It is of interest to note that the percentage of deaths attributed to lung cancer in the general population is almost identical with the figure of 1.32% for the finding of lung cancer in a large group of silicotic lungs.

Documentation of the cases of coexistent lung cancer and asbestosis became my next endeavor. For this purpose, I visited Dr. S. Roodhouse Gloyne at the Institute for Social Medicine in Oxford. Dr. Gloyne's studies of the pathology of asbestosis are well known.[19] For many years he has received lungs for review on matters of compensation. Dr. Gloyne generously gave me permission to cite the data in Table 1, which he assembled from lungs that he personally examined in the gross and microscopically. It is to be hoped that a full account of them will be

17. (*a*) Merewether, E. R. A., and Price, C. W.: Report on Effects of Asbestos Dust on the Lungs and Dust Suppression in the Asbestos Industry, London, His Majesty's Stationery Office, 1930 (summarized in J. Indust. Hyg. & Toxicol. **12**:117, 1930, and in Tubercle **15**:69-81, 109-118, and 152-159, 1933-1934); (*b*) ibid., p. 10, Table 3; (*c*) ibid., p. 14, Table 7.

18. Gloyne, S.: The Morbid Anatomy and Histology of Asbestosis, Tubercle **14**:445-455, 493-497, and 550-558, 1932-1933; Asbestosis, in Silicosis and Asbestosis, edited by Lanza, A. J., New York, Oxford University Press, 1938, pp. 225-244.

published from a manuscript that was in preparation at the time of his recent death.[19]

In addition to the material of Table 1, Dr. Gloyne also examined the lungs of 169 persons without pneumoconiosis but employed in the same set of industries as those included in Table 1. Among these, he found 14 who had primary lung cancer (8.3%). The lungs of 11 asbestos workers who had no asbestosis (either in the gross or microscopically) were negative for carcinoma. The 17 cases of cancer in asbestotic lungs (Table 1) were about equally distributed between men and women (10 men, 7 women), whereas in the normal population in England the ratio is said to be 4 men to every woman with cancer of the lungs. In addition to the higher incidence of cancer in asbestotic lungs, Dr. Gloyne felt that this difference in the sex ratio afforded evidence for an occupational factor.

It will be apparent that the lung cancer rate of 8.3% found in the 169 individuals without pneumoconiosis and the rates of 5.1 to 8.9% in the groups with pneumoconioses other than asbestosis are much higher than the rate of 1.36% estimated for the general population on the basis of death certificates and the rate of 1.32% found from pathological examination of the large group of silicotics previously

TABLE 1.—*Incidence of Primary Lung Cancer in Groups with Various Types of Pneumoconiosis (Data of S. Roodhouse Gloyne)*

| Occupational Group | Persons with Pneumoconiosis | | |
|---|---|---|---|
| | Total Number | Number with Primary Lung Cancer | Percentage with Primary Lung Cancer |
| Iron and steel workers | 78 | 4 | 5.1 |
| Pottery workers | 340 | 19 | 5.6 |
| Coal miners | 288 | 19 | 6.5 |
| Stonemasons | 96 | 8 | 8.9 |
| Asbestos workers | 121 | 17 | 14.0 |

described. It is thus probable that the higher rates reflect closer study. Despite this elevation of the base line for comparison, the rate in the asbestosis group continued to stand out. Dr. Gloyne stated that of the total number of lung cancers in his series, 7.5% were discovered only on microscopic examination. These were scattered through the various groups.

The type of cancer[20] and the degree of asbestosis in the 17 cases of the asbestosis group are given in Table 2. Only one individual (M. S.) had evidence of tuberculosis. In the 922 cases comprising the whole of the pneumoconiosis group (Table 1), 20% showed tuberculosis. Dr. Gloyne made a special search for precancerous changes in asbestotic lungs and did not detect any. Desquamation of bronchial epithelium was occasionally seen, but squamous cell metaplasia was not found save in the cancers themselves. It will be noted from Table 2 that the degree

19. A brief posthumous publication has appeared (Gloyne, S. R.: Pneumoconiosis: A Histological Survey of Necropsy Material in 1,205 Cases, Lancet 1:810-813, 1951).

20. Through the courtesy of Dr. K. F. W. Hinson, of the London Chest Hospital, we have received lobes from six lungs of Dr. Gloyne's series. This material was examined by Dr. Douglas A. Sunderland, of Memorial Hospital, New York. Two cases (C. W. and J. W.) classified as squamous cell cancer by Dr. Gloyne were interpreted as terminal bronchiolar ("alveolar cell") carcinoma by Dr. Sunderland.

of asbestosis in the group of cancerous lungs was recorded as "moderate" or "extensive" in every case except one, where it was "mild." The estimation of the degree of asbestosis was made in every instance by the same observer (Dr. Gloyne).

The 17 cases of coexistent lung cancer and asbestosis studied by Dr. Gloyne were assembled over a period of 20 years (1929 to 1949). All had their exposure to asbestos prior to 1932, the year modern exhaust ventilation devices were adopted in conformance with government regulations. The majority were employed at a plant handling Rhodesian blue and South African (also blue) asbestos. Both these types are more brittle than Canadian white asbestos, hence give rise to more dust. At least one patient (J. I.), however, was stated to have been exposed only to Canadian white asbestos.

I next visited Prof. E. J. King at the British Post-Graduate Medical School in London, where I had the opportunity to examine protocols relating to the lungs

TABLE 2.—*Pathological Findings in 10 Men and 7 Women with Asbestosis and Lung Cancer (Data of S. Roodhouse Gloyne)*

| Patient | Degree of Asbestosis | Type of Cancer |
|---|---|---|
| (Males) | | |
| A. G. | Extensive | "Oat Cell" |
| A. W. | Extensive | "Oat Cell" |
| P. B. | Moderate | Squamous Cell |
| J. G. | Moderate | Squamous Cell |
| J. I. | Moderate | Squamous Cell |
| G. M. | Moderate | Squamous Cell |
| E. T. | Moderate | Squamous Cell |
| J. W. | Moderate | Squamous Cell |
| C. W. | Moderate | Squamous Cell |
| J. P. | Mild | "Oat Cell" |
| (Females) | | |
| H. S. | Extensive | Squamous Cell |
| L. W. | Extensive | Squamous Cell |
| M. C. | Moderate | Squamous Cell |
| E. O. | Moderate | Squamous Cell |
| M. S. | Moderate | "Oat Cell" |
| Le. S. | Moderate | "Oat Cell" |
| R. M. | Moderate | Adenocarcinoma |

of 11 individuals who had been employed in a plant using Canadian white asbestos. The pathological descriptions were made by Dr. C. V. Harrison. Varying degrees of asbestosis were noted in 8 of these 11 lungs; there were 3 cancers, all among the 8 asbestotic lungs. An "oat cell" cancer was found in lungs of one patient (male) with extensive asbestosis. Anaplastic carcinomas were described in two patients (males), in one of whom the degree of asbestosis was moderate; in the other the asbestosis was minimal. The asbestosis ranged from extensive to moderate in the 5 remaining patients in whom this disease was not complicated by cancer. Combining the data of Dr. Gloyne and Dr. Harrison, one finds that in 20 cases of coexistent lung cancer and asbestosis, the degree of asbestosis was "extensive" in 5, "moderate" in 13, and "mild" or "minimal" in 2. The cancer was squamous cell in 11, "oat cell" in 6, anaplastic in 2, and adenocarcinoma in 1. There was no correlation between type of cancer and degree of asbestosis.

I next visited Dr. Hubert Wyers, the medical officer for a company in England engaged in manufacturing asbestos products from blue asbestos mined in Rhodesia

or South Africa. Dr Wyers is the author of a valuable clinical study of asbestosis.[21] He stated that asbestosis was recognized in 1900 and that the industry grew to major stature in the war of 1914–1918. Dr. Wyers has seen only two deaths from asbestosis in people who started to work in the industry after 1932, the year when exhaust ventilation devices were installed. In contrast, he had seen 115 deaths involving asbestosis in persons employed before 1932. He feels that the regulations in regard to safety conditions in the asbestos industry are therefore a great triumph of preventive medicine. The diminution in the severity of the disease in terms of the number of persons affected is further borne out by lessened severity in the individual cases. Prior to 1932 the disease was acute, with deaths sometimes occurring after two years of exposure. The disease as it is now seen is much more chronic. In the 117 cases of asbestosis seen by Dr. Wyers primary lung cancer was found in 17. Dr. Gloyne examined the lungs in these 17 cases, and his pathological diagnoses of the tumors have been given above.

All of the 17 individuals with asbestosis and lung cancer were exposed before 1932. According to Dr. Merewether, the additional 3 cancer patients studied by Dr. Harrison were likewise exposed before 1932. I specifically inquired of Dr. Merewether whether any cases of coexistent lung cancer and asbestosis had been reported in individuals whose exposure had taken place only since 1932. He stated that only one such case has been reported: that of a man employed in the industry between 1935 and 1945. This single case might well be expected as part of the "normal" incidence of lung cancer in any group as large as that employed in the asbestos industry.

In summary, then, I was able to find some information on a total of 21 persons with coexistent lung cancer and asbestosis, of whom only one was a man working under conditions now prevailing in the industry. The additional 10 patients making up the total of 31 described in the Annual Report of the Chief Inspector of Factories for the year 1947 had all been exposed prior to 1932 and I did not attempt to locate autopsy protocols describing them.

It was the consensus of Dr. Gloyne, Dr. Wyers, and Dr. Merewether that the nature of the disease, asbestosis, as seen in England has changed so that it is less common and less severe in individuals whose employment in the industry has taken place only since 1932. It was the consensus that a lung tumor hazard formerly existed in this industry in Great Britain but that there is no evidence to show that such a hazard continues to exist under the working conditions now prevailing.

It should be further noted that in the 1947 factory report Dr. Merewether shows that a mean exposure of 16.5 years, with a range of 1.5 to 40 years, existed in the cases of asbestos workers who succumbed to lung cancer. Individuals beginning their employment in the 1930's are therefore only now reaching the mean age at which tumors might be expected to appear. The size of this group is not known, but the fact that it has thus far provided only a single case of coexistent lung cancer and asbestosis argues that any lung tumor hazard has been greatly diminished, at least in point of time. Whether there will be any significant number of cases with delayed appearance remains to be seen.

*Prof.* King described his experimental studies on the use of alumina in pneumoconioses. In the case of experimental asbestosis, alumina had no beneficial effect

21. Wyers, H.: Asbestosis, Postgrad. M. J. 26:631-637, 1950.

July, 1950, a conference was held at Oxford dealing with cancer in relation to sociological and environmental factors other than occupation. Proceedings of this conference have been published.[51]

## ABSTRACT OF DISCUSSION

DR. PAUL CARTIER, L'Annonciation, Que., Canada: I have been asked to describe our experience at the Thetford Industrial Clinic in Quebec, where we see men engaged in the asbestos mining industry in Canada. Table 3 presents data on eight cases of primary cancer of the lung which we have detected among 4,000 asbestos workers between 1940 and 1950.

In addition to those listed in the table, there was a case in which there was quite a definite clinical and radiological history of cancer of the lung but for which, unfortunately, no autopsy was performed. Also there were three other cases with a strong suspicion in favor of a cancer of the lung but for which no sufficient data are available.

On analyzing these data it seems obvious that many points would need discussion before anyone will be able to establish a causal relationship between these pathological findings and the asbestos factor.

Is it not more logical to think that the same causal factor will produce the same type of tumor, and, therefore, why do we observe such a variety of malignant tumors?

TABLE 3.—*Cases of Carcinoma of the Lungs Detected Among 4,000 Asbestos Workers 1940-1950*

| Patient | Years of Exposure | Years in Industry | Age at Death | Degree of Asbestosis | Type of Tumor |
|---|---|---|---|---|---|
| J. A. | 30 | 34 | 59 | Minimal | Bronchogenic carcinoma |
| A. A. | 25 | 25 | 57 | Minimal | Bronchogenic carcinoma |
| A. L. | 21 | 21 | 51 | Advanced | Mediastinal lymphosarcoma with pulmonary metastasis |
| L. G. | 11 | 17 | 54 | None | Bronchogenic carcinoma |
| L. L. | 10 | 26 | 65 | Minimal | Pleural mesothelioma* |
| E. G. | 2 | 14 | 64 | None | Bronchogenic carcinoma |
| C. B. | None significant | 27 | 59 | .... | Bronchogenic carcinoma (thoracotomy) |
| W. C. | None | 29 | 65 | None | Pleural mesothelioma* |

* "Standard Nomenclature of Diseases and Operations" published by the American Medical Association (New York, The Blakiston Company, 1942) suggests the term "mesothelial sarcoma."

If for a moment we may assume that the asbestos fibers might produce a bronchogenic carcinoma in asbestotic employees with significant exposure, then only two cases of the series would serve as evidence because the cases of mesothelioma or lymphosarcoma and cases without exposure or without asbestosis do not have the conditions required.

As a last remark, it would appear necessary that any statistics on occupational cancer of the lung, to be conclusive, should indicate the precise variety of lung cancer.

MR. EDWARD A. LEW, New York: The difference in the frequency of lung cancer in persons with asbestotic lungs as compared with the large group of silicotics provided by the Pneumoconiosis Board seems impressive. However, one might wonder whether the two groups had been examined for cancer with equal care. I am impressed by the fact that when different groups of lungs were studied by the same observer, Dr. Gloyne, the differences in frequency of lung cancer were much less. If we restrict our attention solely to Dr. Gloyne's series, I am not sure that the differences are statistically significant.

DR. A. J. LANZA, New York: I think it is important to distinguish between cases of clinically recognizable and fatal lung cancer, on one hand, and cases in which the diagnosis of lung cancer has been made as more or less of an incidental finding at autopsy, on the other. The English claim for an association between lung cancer and asbestosis has been based, it seems to me, on data obtained from lungs that a pathologist has searched with a microscope. I wonder how many

51. Conference on Geographical Pathology and Demography of Cancer. J. Nat. Cancer Inst. **11**:627-662, 1950.

cases of lung cancer would be found if lungs from any sort of population were subjected to the same minute scrutiny?

DR. SMITH: In regard to Dr. Cartier's query as to the significance of different types of lung cancer, it may be pertinent to note that a diversity of tumors was found in the lungs of chromate workers reviewed by Dr. Anna Baetjer. Experimentally, the polycyclic hydrocarbons evoke a great variety of tumor types. If asbestos is carcinogenic, I would not expect to see it produce only one type of tumor. I am interested in your observation of two cases of pleural mesothelioma. This is a rather rare tumor. In examining pathological material sent us from England by Dr. Hinson, we found among six cancerous asbestotic lungs two presenting alveolar cell carcinoma. These tumors are often diagnosed as "pleural mesothelioma." I should very much like to exchange slides with you.

In reply to Mr. Lew and Dr. Lanza, it was my understanding that the English cases of silicosis and their cases of asbestosis were handled in the same general fashion through the Pneumoconiosis Board and that the lung cancer rate found in silicotics could therefore serve as a reasonably satisfactory control for the lung cancer rate in cases of asbestosis. In Dr. Gloyne's series of 81 cases of lung cancer in the several pneumoconiosis groups and in the control group, the tumor was evident in the gross in all except 6. Some of his material was destroyed during the bombing of London, but his recollection was that all of the cancers in asbestotics were recognizable in the gross.

DR. JOHN L. POOL, New York: Have experimental studies thrown any light on the question of lung cancer in relation to asbestosis?

DR. SMITH: In 1941, Nordmann and Sorge in Germany claimed to have produced cancer in the lungs of mice by exposing them repeatedly to asbestos dust. Their statement that cancer had resulted in 20% of their exposed animals is occasionally quoted. Actually, their "20%" figure referred only to two mice, one of which had a type of tumor that occurs commonly as a spontaneous growth in mice. The other they considered to be a squamous cell carcinoma, but their photograph does not impress me as that of epidermoid carcinoma. It seems rather to show merely an area of squamous cell metaplasia.