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Histopathologic Classification of Bronchogenic Carcinomas among a Cohort of Workers Occupationally Exposed to Beryllium

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Pathology specimens were examined and classified according to WHO criteria for 27 of 47 individuals identified by death certificate diagnosis as having died from lung cancer, among a cohort of 3055 white males occupationally exposed to beryllium. Twenty-five of the 27 lung tumor specimens were verified as bronchogenic carcinoma: 5 epidermoid; 9 small cell anaplastic; 6 adenocarcinoma, bronchogenic type; 2 adenocarcinoma, bronchiolar–alveolar type; and 3 large cell undifferentiated. Pathology and/or autopsy reports, available for an additional 10 of the 47 individuals, substantiated the death certificate diagnosis.

INTRODUCTION

In a paper published elsewhere in this volume, Wagoner *et al.* identified by death certificate diagnosis 47 individuals who died from lung cancer among a cohort of 3055 white males occupationally exposed to beryllium. This was demonstrated to be a statistically significant excess number of deaths from lung cancer, when compared to the calculated number of expected lung cancer deaths based upon age and cause-specific death rates for the white male population of the United States. This report describes the effort made to collect and review all available clinical data and the histopathology of the lung tumors of those 47 individuals.

MATERIALS AND METHODS

Pathology reports and pathology specimens (microscope slides and/or tissue blocks) were requested from all available sources of such information, for the 47 individuals in the study cohort who were identified from death certificate diagnosis to have died from lung cancer (Wagoner *et al.*, 1980). Microscope slides of tumor specimens were reviewed by one of the authors (Y.S.). Tumor histology was classified according to WHO criteria (Kreyberg, 1967). Smoking histories, where available, were determined from the clinical records, and generally were the result of casual questioning by the physician about social habits.

RESULTS

Microscope slides of tumor specimens (or tissue blocks from which slides could be made) adequate to verify the death certificate diagnosis of pulmonary malignancy and to determine the tumor cell type, were obtained for 27 of the 47 individuals (see Table 1). Pathology or autopsy reports adequate to substantiate a

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TABLE 1
STATUS OF RECEIPT OF INFORMATION TO SUBSTANTIATE DEATH CERTIFICATE DIAGNOSES OF BRONCHOGENIC CARCINOMA

Individuals in cohort with death certificate diagnosis of bronchogenic cancer	47	
Pathology specimens received for review		27
Pathology and/or autopsy reports received (no pathology specimens)		10
Clinical history received (no pathology reports or specimens received)		5
No clinical history, pathology reports or specimens received		5
Total	47	47

clinical diagnosis of pulmonary malignancy were received for an additional 10 individuals, for whom pathology specimens were not available. Clinical histories alone were available for another 5 individuals, for whom pathology or autopsy reports and specimens were not available. Clinical information or pathology specimens were not available for 5 individuals.

All individuals for whom pathology specimens were received were verified as having had a malignancy within the lung (see Table 2). The primary site of that malignancy was identified as the lung for 25 of those 27 individuals. Five of these malignancies were epidermoid carcinomas (WHO classification I), 9 were small cell anaplastic carcinomas (WHO classification II), 6 were adenocarcinoma, bronchogenic type (WHO classification III-1), 2 were adenocarcinoma, bronchiolar–alveolar type (WHO classification III-2), and 3 were large cell undifferentiated carcinomas (WHO classification IV). Smoking histories were determined for 17 of these 25 individuals. All 17 were either current (at the time of hospitalization) or former smokers. Double primary tumors were identified for two of the individuals who were verified as having had primary lung carcinoma, cases 12 and 18. For 2 of the individuals (cases 26 and 27), the primary site was outside the lung (case 26) or unknown (case 27).

Pathology and/or autopsy reports were available for an additional 10 individuals (see Table 3). Histologic diagnoses were available for 7 of the 10 individuals, and included 5 epidermoid carcinomas, 1 small cell anaplastic carcinoma, and 1 adenocarcinoma with the primary site clinically uncertain. Smoking histories were available for 4 of these individuals. All 4 were smokers.

No information to assess the extent of beryllium exposure was available for any

TABLE 2

HISTOLOGY OF CASES IDENTIFIED BY DEATH CERTIFICATE REVIEW AS BRONCHOGENIC CARCINOMA, AMONG THE COHORT OF WORKERS OCCUPATIONALLY EXPOSED TO BERYLLIUM

Case No.	Age at death	Smoking history (as given in clinical history)	Source of pathology specimen	Histology based on examination of pathology specimens submitted for review
1	65	Not stated	Biopsy	Epidermoid (WHO I)
2	76	Former smoker	Biopsy	Epidermoid (WHO I)
3	48	1 ppd × 25 yr	Autopsy	Epidermoid (WHO I)
4	46	1 ppd × 30 yr	Biopsy	Epidermoid (WHO I)
5	66	Heavy smoker	Autopsy	Epidermoid (WHO I)
6	59	Not stated	Autopsy	Small cell anaplastic (WHO II)
7	54	1 ppd	Biopsy	Small cell anaplastic (WHO II)
8	60	1 ppd	Biopsy	Small cell anaplastic (WHO II)
9	63	Not stated	Autopsy	Small cell anaplastic (WHO II)
10	69	Former smoker	Biopsy	Small cell anaplastic (WHO II)
11	61	1/2 ppd	Biopsy	Small cell anaplastic (WHO II)
12	73	Smoker	Autopsy	Small cell anaplastic (WHO II), and Astrocytoma of brain (double primary)
13	62	1 ppd	Biopsy	Small cell anaplastic (WHO II)
14	66	Not stated	Biopsy	Small cell anaplastic (WHO II)
15	62	Occasional smoker	Biopsy	Adenocarcinoma, bronchogenic (WHO III-1)
16	72	Not stated	Autopsy	Adenocarcinoma, bronchogenic (WHO III-1)
17	67	Heavy smoker	Autopsy	Adenocarcinoma, bronchogenic (WHO III-1)
18	68	2 ppd	Autopsy	Adenocarcinoma of lung (WHO III-1) and of colon (double primary)
19	57	1 ppd	Autopsy	Adenocarcinoma, bronchogenic (WHO III-1)
20	42	Not stated	Autopsy	Adenocarcinoma, bronchogenic (WHO III-1)
21	60	1 1/2 ppd	Autopsy	Adenocarcinoma, bronchiolar–alveolar (WHO III-2)
22	50	Not stated	Autopsy	Adenocarcinoma, bronchiolar–aveolar (WHO III-2)
23	55	1 ppd × 40 yr	Autopsy	Large cell undifferentiated (WHO IV)
24	46	Heavy smoker	Autopsy	Large cell undifferentiated (WHO IV)
25	77	Not stated	Autopsy	Large cell undifferentiated (WHO IV)
26	43	Not stated	Autopsy	Adenocarcinoma of pancreas, metastatic to lung
27	48	Not stated	Autopsy	Adenocarcinoma, primary site uncertain

TABLE 3
PATHOLOGY REPORTS OF CASES IDENTIFIED BY DEATH CERTIFICATE REVIEW AS BRONCHOGENIC CARCINOMA, FOR WHOM NO PATHOLOGY SPECIMENS WERE AVAILABLE

Case number	Age at death	Smoking history	Pathology report
28	52	1 1/2 ppd	Biopsy of lymph node: metastatic squamous cell carcinoma
29	59	Not stated	Biopsy of lymph node: metastatic squamous cell carcinoma
30	63	Not stated	Biopsy of lung: anaplastic bronchogenic carcinoma
31	54	Not stated	Autopsy: bronchogenic carcinoma
32	75	Not stated	Cytology: class V squamous cell carcinoma
33	68	2 ppd	Biopsy of lung: oat cell carcinoma
34	68	Not stated	Biopsy of lung: squamous cell carcinoma
35	64	1 ppd	Biopsy of lung: adenocarcinoma in lung
36	57	Not stated	Autopsy: bronchogenic carcinoma
37	48	60 pack years	Biopsy of femur: squamous cell carcinoma

of the 47 individuals in this report. However, 40 of these 47 individuals were employed for less than 5 years at the beryllium production facility under study.

DISCUSSION

Collection of the material which is the subject of this report depended on the cooperation of a wide variety of sources, including individual physicians, hospital medical records rooms, hospital pathology laboratories, etc. Some of the information submitted to NIOSH went as far back as 20 years. Thus, it is not surprising that pathology specimens could be obtained for only 57% (27/47) of the individuals.

The death certificate diagnosis of bronchogenic carcinoma was directly substantiated for 25 of the 27 deaths where pathology specimens were available, and could be substantiated by pathology and/or autopsy reports for 10 of the 15 additional deaths where clinical history and/or pathology reports alone were obtained.

The use of histological cell typing of lung tumors as an epidemiologic marker in the study of certain occupationally related lung cancers has been suggested in previous studies (Kreyberg, 1962; Archer *et al.*, 1974; Figueroa *et al.*, 1973). From the beginning of our efforts to collect this material, it had been hoped that adequate information would be obtained to allow evaluation of the prevalence of histological cell types of lung cancer among persons occupationally exposed to beryllium. Due to the inadequate response rate for the submission of pathology specimens for review, such an evaluation cannot be made. It cannot be assumed that the 20 individuals for whom pathology specimens were not received would necessarily have had a distribution of tumor cell types similar to those 27 individuals for whom pathology specimens were received. While epidermoid carcinomas comprised 20% of the pathology specimens received (5 out of 25 verified bronchogenic carcinomas), epidermoid carcinomas comprised 71% (5/7) of the cancers for which pathology reports alone were available and which listed a tumor cell

type. Thus, the prevalence of histopathological cell types of bronchogenic carcinomas among workers occupationally exposed to beryllium cannot be defined at this time.

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