Occupations and Cigarette Smoking as Factors in Lung Cancer

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This four-year study offers additional evidence tending to connect heavy cigarette smoking with cancer. In addition, it lists several occupations that seem to have some etiological relationship to the disease. They need further study, as it is suggested.

✠ The sharp increase in lung cancer mortality constitutes one of the most spectacular disease phenomena of the past two decades. In the United States the age-adjusted mortality rate for lung cancer climbed from 2.7 per 100,000 population in 1930 to 11.0 in 1948, a more than fourfold increase. In at least one state, California, pulmonary cancer now accounts for more deaths than does pulmonary tuberculosis, and among males aged 45–64 it causes 4 per cent of all deaths.

Attempts to explain this rising mortality as spurious, e.g., as due to improved diagnosis of the disease, do not stand up. The lung cancer death rate—which unfortunately is still our best approximation of incidence rate — has increased two and a half times more rapidly among men than among women. One can hardly presume that physicians have applied diagnostic improvements so much more completely to men than to women. Likewise, the increasing proportion of lung cancer found as a cause of death among autopsies supports the conclusion that we are dealing with a real increase in the disease.[1]

Environmental changes appear to offer the best explanation for the phenomenon. Previously published studies have implicated cigarette smoking [2-5] and certain occupations [6] — especially those involving exposure to radioactive [7] and chromate ores [8] and asbestos [9]—in the causation of lung cancer. However, the number of persons known to have such occupational exposures in the United States is relatively small.

The present investigation was undertaken four years ago: (1) to determine whether any additional occupations might be involved in lung cancer and thus deserve intensive investigation, and (2) to obtain data on the role of tobacco usage in lung cancer.

Methodological Considerations

Definitive study of whether an occupation or cigarette smoking is a causative factor in lung cancer requires that the incidence rate for the exposed group be determined. This rate is then compared with that of a control population, the most acceptable control being all the rest of the population from which the

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exposed group came. Assuming the same diagnostic and reporting standards for both groups, one may thus determine how the chance that a member of an exposed group will develop lung cancer compares with the chance that such a person would develop the disease if he were not a member of the exposed group. If the likelihood of developing lung cancer is substantially increased by being in the exposed group (e.g., a certain occupation) one may conclude that the exposure is a causative factor in the disease. The key to this analysis lies in determining comparative incidence rates for a suspect group and a control population.

But first it is necessary to identify suspect exposed groups. That was the aim of the present study. The importance of pin pointing these groups arises from the fact that incidence studies require assembling sizable populations and observing the occurrence of the disease in them—a large and expensive task. If, for example, data were obtained implicating occupations beyond those already known to be causative factors in lung cancer, one would be justified in assembling populations of the occupational groups and observing them for lung cancer incidence rates—a study which would develop more definite proof of the presence or absence of an etiological relationship.

Several methods of investigation have advanced our knowledge in this sphere. First, is clinical observation of association between a case or a few cases of lung cancer and some exposure, e.g., asbestos. One defect of this method is that such clinical observation depends largely on chance and often involves such small numbers of cases that the validity is questioned. Where made, of course, such observations are helpful.

Another common method of identifying suspect occupations in a highly fatal disease, such as lung cancer, is to note the frequency of the various occupations on death certificates where the disease appears as the cause of death. The frequencies of the occupations on such death certificates may then be compared with those on all death certificates for the general population. If certain occupations appear with much greater frequency on death certificates for lung cancer than on certificates where death is due to other causes, one may conclude that the occupation may be involved and should be intensively investigated. Important achievements may be credited to the use of this method. However, major difficulties with this use of death certificate data arise from the following circumstances: only one occupation may be recorded; while this is supposed to be the "usual occupation," it is often not correctly recorded and duration in the occupation is not recorded. All these circumstances tend to blur the identification of suspect occupations from death certificates.

The method selected in the present study was to determine the lifelong occupational and tobacco-usage history of lung cancer patients (and a control group) by actual interview with the patients. The work history included the number of years engaged, name of company, industry, a description of duties, and listing of products and hazardous materials known to the patient.

Data Collection

Patients observed during 1949–1952 in 11 California hospitals (three county general hospitals, five veteran or military, two university, and one private hospital) comprised the study group. An interviewer especially qualified in occupational analysis obtained the data from each patient in the cooperating hospitals whose condition permitted the interview. The session with each patient often lasted two hours or more, since many details about smoking were

obtained and the information about every occupation was highly detailed. A total of 518 patients who finally had histopathologically proved diagnoses of lung cancer were ultimately included in the analysis.

For every patient in the case series another patient admitted to the hospital about the same time—of the same age (within five years), sex, and race—for a condition other than cancer or a chest disease was chosen in a random manner as a matched "control." Two interviewers, one working in Northern California and one in Southern California hospitals, obtained the data from the lung cancer patient and control patients using the same schedule in identical manner. That interviewer bias did not enter into the determination of tobacco-usage history seems likely, among other reasons, because the results closely parallel those obtained in other investigations where such bias apparently was excluded,[4-5] and because the results for the two interviewers were very similar. It is difficult to conceive how interviewer bias might have affected the occupational data, since both lung cancer patients and control patients mentioned hundreds of occupations and none of these was suspected by the interviewers. Preliminary findings were kept from the interviewers until the end of the data collection.

Method of Analysis

Each record was reviewed by a physician, particularly with respect to the pathologic diagnosis. An industrial hygiene chemist completed the listing of materials usually involved in the occupations mentioned by the patients but not necessarily known to them. Thereafter, the data were coded and tabulations prepared.

Attempts to analyze the data concerning type of industry and exposure to materials already identified as toxic or carcinogenic did not prove fruitful. Hence the major analytical effort with respect to work history went into the data on occupation itself. This had been coded according to the Dictionary of Occupational Titles (2nd ed., 1949), prepared by the Division of Occupational Analysis, U. S. Employment Service, a code with 367 three-digit titles. Particular attention was devoted to the question of years of exposure because present knowledge of carcinogenesis due to environmental agents indicates that duration of exposure and a long latent period are critical factors.

Data on tobacco usage were analyzed so as to reveal the type and degree of smoking, as well as the fact of smoking itself.

Finally, an attempt was made to separate the effects of tobacco usage and occupations which appeared implicated.

Table 1—Age Distribution of Lung Cancer Patients and Controls

Age	Cases			Controls
	Adeno-carcinoma	Other Types of Carcinoma	Total	Total
Total	46	472	518	518
Under 40	3	22	25	26
40–49	6	56	62	59
50–59	19	194	213	213
60–69	14	154	168	169
70 and over	4	46	50	51

Table 2—Sex and Race Distribution of Lung Cancer Patients and Controls

Sex and Race	Cases			Controls
	Adeno-carcinoma	Other Types of Carcinoma	Total	Total
Total	46	472	518	518
Total male	42	451	493	493
White	41	420	461	461
Negro	..	20	20	20
Other	1	11	12	12
Total Female	4	21	25	25
White	3	15	18	18
Negro	1	3	4	4
Other	..	3	3	3

Findings on Smoking

Tables 1 and 2 reveal the distribution of the lung cancer patients according to their biological characteristics — age, sex, race, and the essential similarity of the matched control series in respect to these characteristics.

Tobacco usage by lung cancer patients and the control group is shown in Table 3. Here one may note that 484 (93 per cent) of the cases gave histories of having smoked cigarettes; whereas only 394 (76 per cent) of the controls gave a similar history. No such greater frequency of tobacco usage in other forms (pipe, cigar, chew, and snuff) occurs among the lung cancer patients when compared with the control group. In fact, 68 of the control group used tobacco in a form other than cigarettes exclusively; whereas only 15 of the lung cancer patients did so—relative frequencies which are not much

Table 3—Tobacco Usage During 20 Years Prior to Study Reported by Lung Cancer Patients and Controls

Manner of Using Tobacco	Cases			Controls
	Adeno-carcinoma	Other Types of Carcinoma	Total	Total
Total	46	472	518	518
Total not smoking cigarettes	6	28	34	124
No use of tobacco	4	15	19	56
Tobacco other than cigarettes, only	2	13	15	68
Total smoking cigarettes	40	444	484	394
Cigarettes, only	31	298	329	240
Cigarettes and other	9	146	155	154

Table 4—Amount of Cigarette Smoking During 20 Years Prior to Study Reported by Lung Cancer Patients and Controls

Packages of Cigarettes Smoked per Day	Cases		Controls	
	Number	Per cent	Number	Per cent
Total	518	100	518	100
None	34	7	124	24
< ½	19	4	50	10
½ —	71	14	105	20
1 —	304	59	199	38
2 or more	80	15	22	4
Not recorded	10	2	18	3

different for the nonusers of tobacco in the two series.

This suggestion of an effect by cigarettes only is consistent with other investigations in the field. Some support for the hypothesis that cigarette smoking affects the development of epithelial carcinoma of the lung more than adenocarcinoma may be noted. Six out of 46 (13 per cent) of the cases of adenocarcinoma did not smoke cigarettes; whereas only 28 out of 472 (6 per cent) of the patients with other types of carcinoma, described variously as squamous, epithelial, undifferentiated, did not smoke cigarettes.

One commonly used measure of the amount of exposure to cigarette smoking, the average number of packs smoked per day, appears in Table 4. Seventy-four per cent of all lung cancer patients reported smoking one or more packs of cigarettes on the average per day over the preceding 20 years, compared with a frequency of only 42 per cent among the controls. "Excessive cigarette smoking" (two or more packs per day) occurred almost four times as commonly among the case series as among the control group.

Other items which may indicate the amount of cigarette smoking include the age at which the individual began smoking, whether or not he smokes before breakfast, and whether or not he "inhales." Table 5 reveals that, by all

Table 5—Age of Beginning Cigarette Smoking, Smoking Habits, and "Cigarette Cough" Reported by Lung Cancer Patients and Controls

Cigarette Smoking Characteristics	Cases			Controls		
	Number	Per cent Based on Cigarette Smokers Only	Per cent Based on Total	Number	Per cent Based on Cigarette Smokers Only	Per cent Based on Total
Total	518		100	518		100
Total cigarette smokers	484	100	93	394	100	76
Began 15 years of age	166	34	32	116	29	22
Began 15–24	286	59	55	243	62	47
Began 25 years of age	32	7	6	35	9	7
"Inhale"	449	93	87	327	83	63
"Smoke before breakfast"	373	77	72	229	58	44
"Cigarette cough"	204	42	39	112	28	22

Table 6—Estimated Prevalence Rates * of Lung Cancer per 100,000 Males of Selected Ages and Various Cigarette Smoking Habits

	Number		Estimated Prevalence Rates Quantity Smoked Daily †			Relative Prevalence ‡	
	Lung Cancer	Control	Heavy **	All Quantities	None	Heavy	All Quantities
Patients aged 50–59 years							
1. Doll and Hill	276	275	94	42	7	13	6
2. Wynder and Graham	258	210	117	47	4	27	11
3. Sadowsky, Gilliam, and Cornfield	198	208	87	44	12	7	4
4. Present	213	213	102	46	6	17	7
Patients aged 60–69 years							
1. Doll and Hill	197	199	137	63	0	..	..
2. Wynder and Graham	187	160	138	70	5	29	15
3. Sadowsky, Gilliam, and Cornfield	76	71	44	71	5	9	4
4. Present	168	169	433	78	17	25	5

* Estimated according to the method of Cornfield.[11] Data for studies of Doll and Hill; Wynder and Graham; and Sadowsky, Gilliam, and Cornfield from the latter paper.[12]

† Quantity smoked daily, except for present study, is all forms of smoking expressed as cigarettes, with pipes and cigars converted to their equivalents in cigarettes as follows: 1. Doll and Hill—1 oz. of tobacco a week = 4 cigarettes a day; 2. Wynder and Graham—1 cigar = 5 cigarettes, 1 pipeful = 2½ cigarettes; and 3. Sadowsky, Gilliam, and Cornfield—1 cigar = 10 cigarettes, 1 oz. pipe tobacco = 20 cigarettes. 4. For present study, quantity smoked daily includes only cigarette smoking.

‡ Relative prevalence is the ratio: Heavy—rate among heavy smokers/rate among nonsmokers; all quantities—rate among smokers/rate among nonsmokers.

** Heavy smoking is defined as the following number of cigarettes or equivalents of cigarettes per day:—1. Doll and Hill—50 or more; 2. Wynder and Graham—35 or more; 3. Sadowsky, Gilliam, and Cornfield—41 or more; and 4. present study—40 or more.

of these criteria, the lung cancer patients smoked cigarettes to a greater extent than did the control group. Also, approximately two-fifths of the lung cancer patients stated that they had had a "cigarette cough" usually antedating the onset of their illness by many years; 120 said that they had had a cough for five years or more. The frequency of such "cigarette cough" was only about one-half as great among the control group and only 39 of the control patients indicated that their cough had lasted five years or more.

Significance of Findings on Cigarette Smoking

The data clearly show cigarette smoking to be more frequent and intense among lung cancer patients than among the control group. Our data parallel that of other recent, well controlled studies; all indicate a positive correlation between cigarette smoking and lung cancer, a correlation which increases steadily with the amount of cigarette smoking. One can hardly escape the conclusion of Doll and Hill[4] that "smoking is a factor and an important factor in the production of carcinoma of the lung," and the more recent conclusion of Doll,[10] "The results amount, I believe, to proof that smoking is a cause of bronchial carcinoma."

The cigarette smoker or prospective cigarette smoker may wish to know how much his chances of developing lung cancer are increased by such smoking. Acknowledging that a correlation exists, one may still inquire how many times does cigarette smoking increase the

likelihood of lung cancer? Further, what is that likelihood in absolute terms? To answer these questions definitely would require that records of cigarette smoking for large numbers of persons in the lung cancer age be assembled. These persons would then be placed in categories with respect to cigarette smoking, e.g., nonsmokers, moderate smokers, and heavy smokers. Finally they would be observed for a sufficient length of time to determine the rate of lung cancer among the various categories of cigarette smokers and the nonsmokers. (Such studies are now under way.)

However, statistical devices have been developed for data such as those in the present investigation which, if one is willing to make certain assumptions, yield an answer to the question, how many times does cigarette smoking increase the likelihood of lung cancer? Application of Cornfield's formula [11, 12] to the data from four studies, including the present one (Table 6), indicates that for men aged 50–59 the prevalence of lung cancer is from four to 11 times as great among smokers as among nonsmokers, and from seven to 27 times as great among heavy smokers as among nonsmokers. Similar ratios were found for the 60–69 age group. This formula involves the assumption that in so far as smoking history is concerned, the patients are a representative sample of all lung cancer cases and the controls are a representative sample of all other persons in the general population.

Findings on Occupations

As noted earlier, the records for lung cancer patient and controls showed all

Table 7—Twenty Per cent Sample from Complete List of Occupational Groups [1] in Which There Were at Least 5 Cases or 5 Controls Employed for 5 Years or More

	Occupation	Persons Employed in Occupation at Least 5 Years	
		Cases	Controls
006	Authors, editors, and reporters	7	9
088	Ship captains, mates, pilots, and engineers	8	8
105	Clerks, general office	2	8
155	Canvassers and solicitors	3	11
180	Salesmen to consumers	7	4
227	Waiters and waitresses, except private family	14	10
266	Policemen and detectives, public service	6	3
307	Animal and livestock farmers	6	5
317	Farm hands, animal and livestock	10	10
433	General woodworking occupations, not elsewhere classified	8	7
516	Painters, except construction and maintenance	3	6
524	Brick and stonemasons and tile setters	5	1
532	Construction occupations, not elsewhere classified	45	25
542	Locomotive firemen	3	6
560	Attendants, filling stations and parking lots	10	9
583	Mechanics and repairmen, not elsewhere classified	15	16

Note: Sample randomly selected from the 81 occupation groups which met the stated frequency-duration requirements (at least 5 cases or 5 controls with 5 years or more employment). Occupations classified according to 3-digit categories in the Dictionary of Occupational Titles (2nd ed.). Washington, D. C.: U. S. Employment Service, 1949.

Table 8—Occupation Groups * in Which the Frequency of 5 Year Employment Among Cases Was at Least Twice as Great as Among Controls

	Occupation	Persons Employed in Occupation at Least 5 Years	
		Cases	Controls
016	Engineers, civil	5	1
138	Stock clerks	7	3
266	Policemen and detectives, public service	6	3
430	Lumbermen, raftsmen, and wood choppers	11	5
478	Machine shop and related occupations, not elsewhere classified	8	3
485	Welders and flame cutters	10	1
520	Occupations in production of petroleum	5	2
523	Construction machinery operators, not elsewhere classified	7	3
524	Brick and stonemasons and tile setters	5	1
538	Brakemen, railroad	10	5
570	Firemen, other than process firemen	11	2
573	Cranemen, derrickmen, hoistmen, and shovelmen	15	6
575	Drillers, extraction of minerals and construction	7	2

* Occupations classified according to the Dictionary of Occupational Titles (2nd ed.). Washington, D. C.: U. S. Employment Service, 1949. Includes only occupations in which there were at least 5 cases with 5 years or more of employment.

occupations followed and their durations in years. A listing was prepared of the occupations pursued by at least five patients or controls for five years or more. This listing revealed 81 occupations in this arbitrary frequency-and-duration category.

Table 7 presents a random sample of these occupations and the number of patients and controls who at some time during their work history had been engaged in them for five years or more. It will be noted that among the 518 lung cancer patients seven had worked as authors, editors, or reporters (occupation) for five years or more, and among the 518 controls, nine had been similarly engaged. Relative frequencies of occupation would appear to have the same logical significance as such frequencies of cigarette smoking. The latter is, of course, much more common among both case and control groups than is any single occupation. Hence, the numbers pertaining to any one occupation would be less impressive than in the case of cigarette smoking. However, the frequency with which the lung cancer patients had pursued certain occupations was substantially greater than the frequency with which control patients had pursued these same occupations.

The occupations for which the frequency among cases was at least twice as great as among controls, using the same frequency-duration category as before, appear in Table 8. Such a tabulation, of course, shows the occupations classified according to an arbitrary code which was not devised to reflect common occupational exposures that might be responsible for lung cancer. Further analysis therefore included the detailed examination of records of individual cases and controls and regrouping of occupations according to possible common exposures. For ex-

ample, one occupational group, number 530 (plumbers, gas fitters, and steam fitters) showed 16 cases and 10 controls with a five-year employment history. Examination of these 26 individual records revealed that substantially all the difference between case and control series was due to the steam fitters who had a heavy exposure to asbestos. It was also noted that other types of work involving asbestos occurred more frequently in the employment history of cases than among the employment history of controls. Thus, a new category, including steam fitters, asbestos workers, and boilermakers—all involving exposure to asbestos—was found to occur 10 times among the cases and only one time among the controls.

Table 9 presents the data for occupations grouped according to possibly significant exposures. Although numbers in each of the categories are small, the differences between cases and controls appear to implicate the occupations listed. It is of interest to note that several of those with the most striking differences involve exposure to metallic particles and fumes and products of metallic combustion. This observation tends to corroborate the suggestion of Wynder and Graham [13] that "hot metal" occupations may be involved in lung cancer.

In recent data of Doll [10] the only occupation with an important excess in the cancer group was that directly concerned with the production of gas. Little or no support was found indicating that other occupations suffer special risks. However, Doll's study was based upon experience in England where the employment pattern differs from that in the United States, especially California. Also, Doll used an occupation code of only 76 categories which may have been too coarse to reveal the differences found in the present investigation where a code of 367 categories was used and analysis carried to subgroupings of these.

It may be noted that 77 persons with lung cancer had an exposure of more than five years to suspect occupations (unduplicated count in seven occupation groups) according to the data in Table 9. This number represents a not insignificant proportion of the total (518) lung cancer patients in the entire study.

A further question upon which the present data might be expected to throw some light is the extent to which cigarette smoking and occupations operate

Table 9—Cases and Controls Employed for at Least 5 Years in Selected Occupation Groups *

Occupation	Persons Employed in Occupation at Least 5 Years	
	Cases	Controls
1. Welders and sheet metal workers doing welding	14	2
2. Steam fitters, boilermakers, and asbestos workers	10	1
3. Electric bridge crane operators—metal industry	5	1
4. Occupations in the extraction of lead, zinc, and copper ore	9	3
5. Marine engineers, firemen, oilers, and wipers	12	6
6. Construction and maintenance painters	22	12
7. Cooks, commercial (excluding cannery cooks)	35	21

* Occupation groups based on regrouping according to common occupational exposures after detailed examination of records.

Table 10—Example of Adjustment for Smoking Applied to Welders and Sheet Metal Workers Doing Welding

	Packages of Cigarettes Smoked per Day						
	None	<½	½ —	1 —	2 or more	Not recorded	Total
All cases and controls, male *							
1. Cases	22	16	69	296	80	10	493
2. Controls	110	45	105	193	22	18	493
3. Total	132	61	174	489	102	28	986
4. Proportion of cases among total cases and controls	0.167	0.263	0.396	0.605	0.783	0.357	
Welders and sheet metal workers doing welding, male							
5. Cases	0	0	2	11	1	0	14
6. Controls	1	0	0	1	0	0	2
7. Total	1	0	2	12	1	0	16
8. Expected number of welder cases †	0.167	0.0	0.792	7.260	0.783	0.0	9.002

$$\text{Expected proportion of cases among welders} = \frac{9.002}{16} = 0.563$$

$$\text{Observed proportion of cases among welders} = \frac{14}{16} = 0.875$$

Ninety-five per cent confidence limits ‡ for the proportion $\frac{14}{16} = (0.617, 0.984)$—statistically significant at 95 per cent level.

* Females excluded from total group, since only males are included in groups to which test was applied.

† Obtained by applying the proportion of cases among total cases and controls in each smoking category to the number of welders in that smoking category [line No. 4 × line No. 7].

‡ Hald, A. Statistical Tables and Formulas. New York: John Wiley, 1953.

Note: This test also was applied to all other occupation groups shown in Table 9. The group "steam fitters, boilermakers, asbestos workers" was on the borderline of statistical significance at the 95 per cent level. None of the other groups met the 95 per cent level of statistical significance.

as separate factors in lung cancer. For example, both cigarette smoking and welding appear to be related to the disease, but do welders get lung cancer more frequently merely because as a group they are heavy cigarette smokers? Although data from the present study involve small numbers for many of the occupations, analysis does indicate that welding as an occupation operates as a factor distinct from cigarette smoking in relation to lung cancer (Table 10). The group of steam fitters, boilermakers, and asbestos workers lies on the borderline of statistical significance when the effect of cigarette smoking is controlled. In the other occupational groups the numbers are such that the differences might arise from chance variation more than five times in a hundred.

However, all the occupations listed in Table 9 deserve intensive study to determine their precise relationship to lung cancer. One important step is to assemble populations of individuals employed in these occupations, and with varied smoking histories, in order to observe their lung cancer incidence rates. These rates may then be compared with the rate for the corresponding age-sex group in the general population. One may thus determine

how being in a particular occupational group affects the chances of developing lung cancer and likewise how cigarette smoking modifies these chances.

Conclusion

The data in this study constitute still another link in the chain of evidence connecting lung cancer with cigarette smoking, evidence which the New England Journal of Medicine notes to be "so strong as to be considered proof within the everyday meaning of the word." [14] It is time for those concerned with health education and with the ethics of advertising, at least in health and medical journals, to take note. Further investigation should seek the exact component of cigarette smoke—tar, arsenic, or other—which is responsible.

The data also suggest that several occupations (Table 9), in addition to those previously identified as having an etiological relationship, may be involved in the development of lung cancer. These occupations should now be intensively studied to determine to what extent persons engaged in them suffer a special risk of lung cancer. Thereafter, if an etiological relationship is clearly established, the precise exposure and mechanism responsible should be identified in order that protective measures may be introduced.

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Journal 25 Years Ago

ADDENDUM to the January, 1954 "25 Years Ago." In addition to the articles on the common cold mentioned last month, the 1929 Journal (p. 449) describes an eight-page booklet "That Mean Cold," by present-day associate editor of the Journal, Raymond S. Patterson. It was reportedly his first production as director of health education for the John Hancock Mutual Life Insurance Company, the January issue (p. 94) having reported his appointment as director of health education, Life Conservation Service of that company. Dr. Patterson had already been the author of A.J.P.H.'s "Annotated Public Health Bibliography" for several years, it having first appeared under his by-line in March, 1926.