

Conclusion

It is unsatisfactory that the discovery of a new chemotherapeutic drug has never been based on a rational interference with mechanisms known to operate in the host or the parasite. Ironically some of the more toxic of antibiotics have been used to elucidate membrane and transport functions in the cell and protein synthesis. Progress in molecular biology relating to cell-wall structure and protein synthesis has resulted in a remarkable increase in our understanding of how bacteria are impaired or killed by chemotherapy. Further knowledge in this field may in fact lead to the discovery of an agent based on a rational interference with the function and structure of the tubercle bacillus. In the meantime the empirical search for better agents must be continued.

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Smoking Habits of Men Employed in Industry, and Mortality

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Summary: A study of the relation between smoking habits and lung cancer in male industrial workers over a period of three years has confirmed the earlier findings in doctors that the death-rate from lung cancer correlates closely with the number of cigarettes smoked. Of 54,460 men studied 68.7% were current cigarette smokers. The annual mortality rate from lung cancer was 0.33 per thousand in non-smokers and ex-smokers, and 1.2 per thousand for all cigarette smokers, and higher in heavy smokers.

Heavy cigarette smokers who retained the cigarette in the mouth between puffs ("drooping" cigarette habit) had an annual mortality rate of 4.1 per thousand.

The mortality from coronary thrombosis in smokers was nearly three times that in non-smokers. A mortality gradient with rising consumption of cigarettes was observed.

Some correlation between smoking and cancer of other sites and from non-neoplastic lung disease was observed in older men, but no correlation was found with other cardiovascular diseases and cerebrovascular diseases.

Introduction

The relation between smoking and death from lung cancer and other causes has been extensively studied in British doctors (Doll and Hill, 1954, 1956, 1964), but not, so far, in other sections of the population of this country. The present investigation sets out to examine this problem in men working in British industry. It was possible to do this without mounting a separate survey for the purpose by utilizing data on smoking which had been routinely collected in the course of an earlier research project designed for the evaluation of presymptomatic diagnosis of lung cancer (Brett, 1966, 1968).

Material and Method

The population for study totalled 54,460 men aged 40 and over who had all volunteered for routine x-ray examination in 1960, and had been followed up over a period of three years. These men were drawn at random from 119 industrial establishments in the Greater London Area and the Home Counties. Each examinee for x-ray examination was asked to complete a record card which incorporated a questionnaire on smoking habits. The questions were designed to separate in the first instance current cigarette smokers from current non-smokers

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and to subdivide the current non-smokers into those who had never smoked cigarettes and those who at some time in the past had given up smoking. Those who had given up cigarette-smoking at least one year before the x-ray examination were classified as ex-smokers, while those who stopped smoking less than a year ago were counted as current smokers.

Current cigarette smokers were further analysed by the amount smoked and by their manner of smoking. This was determined by answers to specific questions which are based on a personal observation that some smokers tend to hold a lighted cigarette continuously in the mouth rather than remove it after each puff. We called this peculiarity the "drooping" cigarette, a habit that to our knowledge has not been investigated before. Those who sometimes removed and sometimes retained the cigarette between puffs were listed as a "mixed" group. The information on smoking habits was subsequently related to the deaths that had occurred in this population during the three years of study. The cause of death was established in each case from hospital records and the General Register Office at Somerset House.

The survey was carried out by the Mass Radiography Service of the N.W. Metropolitan Region.

Results

Smoking Habits

The population under review has been divided according to three basic smoking habits, and these in turn were related to each of the age groups (Table I). It can be seen that pipe smokers are included among non-smokers. This was done because their relatively small number (821) did not justify separate analysis, and they were incorporated among non-smokers rather than smokers in order to preserve cigarette smokers as a homogeneous group for further study.

TABLE I.—Observed Population by Age and Basic Smoking Habits

Age	Non-smokers (including Pipe Smokers)		Ex-smokers		Smokers		Total Observed	
	No.	%	No.	%	No.	%	No.	%
40-44	1,757	13.3	2,269	17.2	9,206	69.5	13,232	24.3
45-49	1,832	12.6	2,602	18.0	10,053	69.4	14,487	26.6
50-54	1,343	11.3	2,305	19.3	8,268	69.4	11,916	21.9
55-59	907	10.2	1,922	21.9	6,001	67.9	8,830	16.2
60-64	491	10.5	1,053	22.8	3,101	66.7	4,645	8.5
65-69	160	13.8	284	24.5	713	61.7	1,157	2.1
70+	40	20.5	47	24.0	106	55.5	193	0.4
Total	6,530		10,482		37,448		54,460	100.0
Percentage of total population	12.0		19.3		68.7			

It was of interest that with advancing age the proportion of non-smokers registers first a fall and then a rise, while ex-smokers steadily increase and cigarette smokers decline with age.

A comparison with British doctors surveyed in 1951 and again in 1958 (Doll and Hill, 1954, 1964) shows discrepancies in smoking habits which can only partly be explained by different methods of study. There were considerably more pipe smokers in doctors—11.6% in 1951 and 13.2% in 1958—than in industrial workers (1.5%), but fewer cigarette and mixed smokers—55.6% in 1951 and 43.3% in 1958—compared with 68.7% in the present series. The considerable drop in smokers among doctors between 1951 and 1958 indicates that reports on a correlation between smoking and lung cancer had a greater impact on the medical profession than on the industrial population.

The difference in the proportion of non-smokers was less striking—16.9% in doctors as against 12% in industrial workers.

A sample survey conducted in 1961 by the Tobacco Research Council (Todd, 1966), on the other hand, shows fewer discrepancies in smoking habits. In comparable age groups there were about 18% ex-smokers and approximately 69% cigarette smokers, not very different from the corresponding figures of 19.3% and 68.7% in industrial employees. Though the estimated proportion of pipe smokers in Todd's survey was still higher at 5.4% than in ours, when combined with the 9.1% of non-smokers the total of 14.5% was fairly close to the 12% of non-smokers (as defined) in this series.

Table II shows that 11.9% of all cigarette smokers smoked heavily (25 or more cigarettes per day), while light (1-14 cigarettes) and medium smokers (15-24 cigarettes) are divided in almost equal proportions. These figures differ from those in doctors (Doll and Hill, 1964) and also from those reported by Todd (1966). In both these surveys the proportion of heavy smokers was considerably higher (25%) and of light and medium smokers correspondingly lower than in our series. Taking these figures at their face value it seems that there is a real difference between the medical and industrial populations in the amount smoked, with doctors being, surprisingly, the heavier smokers. This finding could reflect the difference in economic status between the two groups. On the other hand, it cannot be excluded—and Todd's figures appear to support this—that the industrial population sample may have understated the number of cigarettes smoked.

TABLE II.—Individual Smoking Habits of Cigarette Smokers

	Cigarettes Consumed per Day						Percentage of Total
	1-14		15-24		25 and Over		
	No. Observed	%	No. Observed	%	No. Observed	%	
Always removes cigarette after each puff	12,685	74.2	11,694	73.8	2,840	63.2	72.7
Always keeps cigarette in mouth between puffs (drooping cigarette)	2,167	12.7	2,130	13.4	1,076	24.0	14.4
Mixed	2,238	13.1	2,044	12.8	574	12.8	12.9
Total	{No. 17,090 % 45.8	100.0	{No. 15,868 % 42.3	100.0	{No. 4,490 % 11.9	100.0	100.0

"Drooping" Cigarette Habit.—Reference has been made earlier to questions related to the manner of smoking. Table II shows that 72.7% of smokers removed the cigarette after each puff, that 14.4% did not (drooping cigarette), and that 12.9% adopt sometimes one and sometimes the other mode of smoking (mixed). It can also be seen that the drooping cigarette habit becomes more common with rising consumption of cigarettes. Nearly twice as many heavy smokers (24%) belonged to this category as light (12.7%) or medium smokers (13.4%).

Mortality

In Table III the mortality experienced by the population under study is related to its causes. Coronary thrombosis was by far the most common cause of death (39%), and the annual

TABLE III.—Cause of Death in Observed Population During Three Years

	No. of Deaths	Percentage of Total	Annual Rate per 1,000
Lung cancer	150	13.9	0.9
Coronary thrombosis	422	39.0	2.7
Other cardiovascular diseases and cerebrovascular diseases	165	15.3	1.0
Cancer other than of the lung	186	17.2	1.1
Respiratory diseases other than lung cancer	75	7.0	0.5
Miscellaneous causes	82	7.6	0.5
Total	1,080	100.0	0.6

TABLE IV.—Annual Lung Cancer Mortality in Cigarette Smokers by Age and Amount Smoked

Age	1-14			15-24			25 and Over		
	No. Observed	No. of Deaths	Rate per 1,000	No. Observed	No. of Deaths	Rate per 1,000	No. Observed	No. of Deaths	Rate per 1,000
40-44	4,037	2	0.2	4,077	2	0.2	1,092	1	0.3
45-49	4,318	3	0.2	4,506	10	0.7	1,229	5	1.3
50-54	3,651	5	0.5	3,512	18	1.7	1,105	7	2.1
55-59	2,931	12	1.4	2,402	19	2.7	668	8	4.0
60-64	1,662	11	2.2	1,109	8	2.4	330	3	8.0
65-69	420	6	4.7	229	5	6.3	64	3	22.0
70+	71	1		33			2		
Total	17,090	40	0.8	15,868	62	1.3	4,490	33	2.4

TABLE V.—Annual Lung Cancer Mortality by Amount Smoked and by Individual Habits of Smokers

Mode of Smoking	1-14			15-24			25 and Over		
	No. Observed	No. of Deaths	Rate per 1,000	No. Observed	No. of Deaths	Rate per 1,000	No. Observed	No. of Deaths	Rate per 1,000
Always removes cigarette after each puff	12,685	24	0.7	11,694	38	1.1	2,840	14	1.6
Always keeps cigarette in mouth between puffs (drooping cigarette)									
Mixed	2,238	9	1.3	2,044	12	1.9	574	6	3.4
Total	17,090	40	0.8	15,868	62	1.3	4,490	33	2.4

mortality from this disease (2.7 per thousand) was three times that from lung cancer. Cancer accounted for 31.1% of all deaths, of which 13.9% were attributed to lung cancer, with an annual mortality of 0.9 per thousand. Respiratory diseases other than cancer of the lung accounted surprisingly for only 7% of all deaths.

Lung Cancer

The annual lung cancer mortality rate was 1.2 per thousand in cigarette smokers and 0.3 per thousand in both non-smokers and ex-smokers. The ratio of annual lung cancer mortality from smokers to non-smokers or ex-smokers was therefore of the order of 4:1. Since the small number of deaths (6) in non-smokers does not really support a calculation of reliable mortality rates, all that can be said is that in this series lung cancer mortality was several times greater in cigarette smokers than in non-cigarette smokers.

The correlation of mortality with age and with amount smoked is shown in Table IV. It can be seen that the level of mortality from lung cancer increases with rising consumption of cigarettes. Thus heavy smokers have a death rate three times that of light and twice that of medium smokers, but eight times that of non-smokers. Table IV also shows a distinct mortality gradient with the amount smoked for all but the youngest (40-44) age groups. In age groups 50 and over the mortality in heavy smokers was four times that in light smokers. The annual death rate increases also with age, irrespective of the amount smoked; this increase occurs earlier and more abruptly in heavy than in light or medium smokers.

It was of interest to see that the death rate from lung cancer is influenced not only by the amount smoked but also by the manner of smoking (Table V). The highest mortality risk is clearly among those who both smoked heavily and belonged to the drooping cigarette category. In this group the ratio to non-smokers and ex-smokers is of the order of 14:1. The gradient of mortality with amount smoked remains evident whatever the manner of smoking, but is distinctly lower in those who remove their cigarette after each puff, with the mixed group holding an intermediate position. It would be of interest to discover whether a similar subgroup could be identified elsewhere, as this could perhaps contribute to the understanding of why some countries, despite similar or higher consumption of tobacco, have a lower lung cancer mortality (Eastcott, 1957; Dean, 1959). To elucidate whether drooping involves a greater

measure of inhaling compared with the removal of the cigarette after each puff would need special investigation, for which this study was not designed.

Other Causes

For this group of diseases the age specific annual mortality was calculated in relation to two larger denominators—namely, age groups 40-54 and 55 and over. Table VI shows that in coronary thrombosis a gradient of mortality from non-smokers to smokers and in smokers to the amount of tobacco consumed was evident for each of the age groups. The mortality risk in smokers was twice that in non-smokers of all ages and almost three times greater in heavy smokers. The death rate started, as expected, at a higher level in the older persons irrespective of their smoking habits, and for this reason the mortality ratio between non-smokers and smokers was 1:3 in the younger and only 1:2 in the older age groups. It was of interest that in the older person the death rate was not materially reduced by giving up smoking or by smoking fewer cigarettes.

In cerebrovascular and cardiovascular diseases (other than coronary thrombosis) the mortality gradient was related to age, but not to smoking.

In cancer other than of the lung rising mortality with increasing consumption of cigarettes was evident only in the older age groups. There was no significant difference in the death rate between non-smokers and smokers.

In the group of respiratory diseases, other than lung cancer, cor pulmonale has been included. It can be seen that in the older age groups mortality was slightly higher in smokers than in non-smokers.

In the group of miscellaneous diseases, in which individual components were represented by too few cases to warrant a separate analysis, no correlation between smoking and mortality could be observed.

Discussion and Conclusions

Since it was the object of this investigation to determine whether the correlation between cigarette-smoking and mortality from lung cancer and other diseases observed in British doctors applied equally to industrial workers, it was essential to compare the results with the earlier findings of Doll and Hill. Strict comparisons of surveys of this kind are not always

TABLE VI.—*Annual Mortality from Other Causes Related to Age and Smoking Habits*

Cause	Age	Non-smokers		Ex-smokers		Smokers—Cigarettes per Day					
		Deaths	Rate per 1,000	Deaths	Rate per 1,000	1-14		15-24		25 and Over	
						Deaths	Rate per 1,000	Deaths	Rate per 1,000	Deaths	Rate per 1,000
Coronary thrombosis	40-54	13	0.9	21	1.0	58	1.6	68	1.9	27	2.6
	55+	15	3.1	50	5.0	77	5.0	72	6.3	21	6.7
	Total	28	1.3	71	2.3	135	2.6	140	2.9	48	3.6
Other cardiovascular and cerebrovascular diseases	40-54	8	0.5	10	0.5	22	0.6	19	0.5	6	0.6
	55+	11	2.3	20	2.0	36	2.3	22	1.8	11	3.3
	Total	19	1.0	30	1.0	58	1.1	41	0.9	17	1.3
Cancer other than of the lung ..	40-54	17	1.0	14	0.7	14	0.4	28	0.8	6	0.6
	55+	8	1.7	19	1.9	30	2.0	35	3.1	15	4.7
	Total	25	1.3	33	1.0	44	0.9	63	1.3	21	1.6
Respiratory diseases other than cancer of the lung	40-54	2	0.1	1	0.05	8	0.2	8	0.2	4	0.4
	55+	3	0.6	6	0.6	21	1.4	22	2.0	—	—
	Total	5	0.3	7	0.2	29	0.6	30	0.6	4	0.3
Miscellaneous causes	40-54	3	0.2	7	0.3	16	0.4	11	0.3	4	0.4
	55+	6	1.2	4	0.4	18	1.2	10	0.9	3	0.9
	Total	9	0.5	11	0.3	34	0.7	21	0.4	7	0.5

possible, because differences in method of study are quite often reflected in different sets of data for analysis. There were, for instance, intentionally fewer smoking categories in this series than in doctors; there were for obvious reasons more older men among doctors than in a working industrial population in which the retiring age seldom exceeded 65 years. There was also the considerable discrepancy in the proportion of pipe smokers which permitted a separate analysis of this category in doctors but not in workers. The higher percentage of cigarette smokers among industrial workers and the surprisingly higher proportion of heavy smokers in doctors were other points of divergence between the two groups.

These differences in smoking habits have, however, had little effect on the basic problem with which the comparison of the two studies is concerned. The discrepancy between the levels of lung cancer mortality in non-smoking doctors (0.07 per thousand) and in non-smoking workers (0.3 per thousand) was obviously responsible for the considerable difference between the mortality gradients from smokers to non-smokers (10:1 and 4:1 respectively) in the two populations. Yet when it is considered that the mortality levels in non-smokers were calculated on the basis of a very small number of deaths the difference between the gradients may not be as significant as the figures suggest. On the other hand, the gradients of lung cancer mortality from ex-smokers to smokers and in smokers by amount smoked are comparable in the two populations. The death rates of 0.3, 0.8, 1.3, and 2.4 per thousand for ex-smokers, light, medium, and heavy smokers respectively are fairly close to those of 0.24, 0.54, 1.39, and 2.27 per thousand in doctors (Doll and Hill, 1964). This similarity showed that the correlation between cigarette-smoking and death from lung cancer had the same significance for British industrial workers as for British doctors.

The discovery of a hitherto unknown high-risk category among cigarette smokers in the shape of those addicted to a drooping cigarette was of interest and justified the effort in putting special questions to the men surveyed in this study.

It is in this group of heavy smokers that mortality from lung cancer was highest (4.1 per thousand). This finding probably merits further study. The level of mortality from coronary thrombosis was for all smoking categories considerably higher in doctors than in industrial workers. But the gradient from heavy smokers to non-smokers, less than 2:1 in doctors and almost 3:1 in industrial employees, stands out more sharply in this series than that of Doll and Hill. It was of interest that in both studies the risk of dying from coronary thrombosis was only slightly lower for the older ex-smoker than for the older smoker.

No evidence was found in either study of a correlation between smoking and death from other cardiovascular or cerebrovascular diseases.

The level of mortality in relation to smoking habits was, for the group of respiratory diseases other than cancer of the lung, considerably lower in our population than in doctors. This is difficult to explain. The gradient of mortality with smoking, though small, was evident in the older age groups of our series, but was more marked in doctors.

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