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CHAPTER 2

Smoking and Chronic Bronchopulmonary Diseases (Non-neoplastic)

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INTRODUCTION

PURPOSE OF THIS REPORT

This report reviews additional pertinent data relative to smoking and chronic bronchopulmonary diseases—specifically chronic bronchitis and pulmonary emphysema.

The reader is referred to the Surgeon General's 1964 Report (68) and recent textbooks for background information on the chemistry of tobacco smoke, the metabolism and toxicity of specific components of tobacco smoke, the physics of its retention in the air passages and the lungs, and the mechanics of pulmonary function.

DEFINITIONS

The scope of this chapter will be limited to emphysema and chronic bronchitis and it may be useful to present definitions of both terms. There have been many definitions of chronic bronchitis and emphysema. Those used in the Surgeon General's 1964 Report had been proposed by the American Thoracic Society in 1962 (37). With the increasing public health interest in chronic bronchopulmonary disease, attempts have been made to develop precise definitions to categorize these diseases and to isolate them satisfactorily from other pulmonary conditions. A task force sponsored by the Chronic Respiratory Diseases Control Program of the Public Health Service and the National Tuberculosis Association deliberated this together with related problems for a week in October 1966. They adopted the following definitions (71):

Chronic bronchitis is a clinical disorder characterized by excessive mucous secretion in the bronchial tree. It is manifested by chronic or recurrent productive cough. The diagnosis of chronic bronchitis can be made only if other bronchopulmonary or cardiac disorders are excluded as the cause for these symptoms. The predominant pathologic change is hypertrophy and hyperplasia of the mucous secreting glands in the trachea and bronchi.

Pulmonary emphysema is an anatomic alteration of the lung characterized by destruction of alveolar walls accompanied by abnormal enlargement of the air spaces distal to the terminal, nonrespiratory bronchiole."

These definitions will be used to describe chronic bronchitis and emphysema as understood in the present report. They are being used

to emphasize the lack of progress in defining the two conditions for purposes of differentiating them from other diseases of the lung. Reference may be made to the Surgeon General's 1964 Report where nearly identical definitions will be found.

Inability to distinguish between chronic bronchitis and emphysema has hampered medical research and exchange of information. The P.H.S.-N.T.A. task force report states further:

"Although patients having only chronic bronchitis tend to have more cough and sputum than do those having only pulmonary emphysema, the array of symptoms, physical findings, and pulmonary physiologic abnormalities are similar in both diseases.

"Chronic bronchitis and emphysema coexist in many patients * * *"

This statement may help to explain some of the difficulties encountered by research workers in studying these diseases and why the researchers are limited to describing symptoms and signs observed in the populations under investigation. It may also explain why it is difficult to distinguish these conditions in the present report which seeks to record the research findings related to smoking and chronic respiratory disease published since the Surgeon General's 1964 Report. Research findings on both diseases are not considered separately in this report but are grouped in population studies, pathology studies, and animal experiments. Additional considerations pertinent to pulmonary emphysema are then provided.

CHRONIC BRONCHOPULMONARY DISEASE MORTALITY¹

Mortality from chronic bronchopulmonary diseases has continued the upward trend well established at the time of publication of the conclusions cited in the Surgeon General's 1964 Report. Deaths in the United States from emphysema or chronic bronchitis or both have risen steadily from about 3,000 in 1950 to more than 20,000 in 1964, as can be seen in table 1.

TABLE 1.—*Mortality from emphysema and/or chronic bronchitis (ISC codes 501, 502, 527.1)*

Year	Number of deaths	Year	Number of deaths	Year	Number of deaths
1964.....	20, 208	1959.....	10, 433	1954.....	4, 877
1963.....	19, 443	1958.....	9, 328	1953.....	4, 657
1962.....	15, 915	1957.....	8, 136	1952.....	3, 846
1961.....	13, 302	1956.....	6, 535	1951.....	3, 660
1960.....	12, 426	1955.....	5, 616	1950.....	3, 157

Source: Vital Statistics of the United States, 1950-1964 (70).

¹ All death rates throughout this chapter are per 100,000 population, unless otherwise indicated.

The increase and aging of the population during the same period does not account for this rise. Age-adjusted mortality rates for emphysema without mention of chronic bronchitis increased about ten times for men, from 1.3 per 100,000 in 1950 to 12.6 in 1964. A similar, although perhaps somewhat less dramatic, increase occurred among women, from 0.2 per 100,000 in 1950 to 1.6 in 1964. Death rates from chronic bronchitis rose less precipitously, doubling during the same period (69, 70). How much of this increase is the result of improved diagnosis of these diseases and how much the result of a true change in mortality patterns cannot be determined at the present time. Associations have been demonstrated between these conditions and smoking.

POPULATION STUDIES

Included in this broad category are investigations that collected information from a group or groups of persons either by a series of questions, by some form of physical examination, or by a review of recorded data such as hospital records and death certificates.

PROSPECTIVE STUDIES

In the Surgeon General's 1964 Report, findings from seven prospective studies were presented. Additional data have been reported from four of these investigations in the past 3 years. Information relevant to smoking and chronic respiratory disease will be summarized here.

The study of mortality among policyholders of U.S. Government Life Insurance policies available to persons who served in the Armed Forces between 1917 and 1940 was initiated in 1952. Almost all the 293,658 policyholders were white males. Recently Kahn (44) published a report that included all deaths from July 1954 through December 1962, a period of 8½ years.

The relation of cigarette smoking to death from bronchitis and emphysema is presented by mortality ratios in table 2 and by specific risk of mortality in table 2A. Given the definitions previously cited, these tables also illustrate the difficulties in separating these diseases. The first row of table 2 gives combined mortality ratios and the next two rows give the same data in an attempt to delineate the specific diseases. Mortality ratios are given by the number of cigarettes smoked per day at the time the men were enrolled in the study. Mortality from these diseases is much higher among cigarette smokers than among those who never smoked and rises with the number of cigarettes smoked daily. The ratios are much higher for emphysema alone than for chronic bronchitis with or without mention of emphysema.

A similar study of veterans was begun in Canada in 1955. Answered questionnaires were returned by nearly 78,000 men whose subsequent mortality for a period of 6 years was recently analyzed by Best and

his associates (12). Deaths from chronic bronchitis and emphysema have been summarized in table 3 which gives mortality ratios by the number of cigarettes smoked each day. Here, again, the mortality is much higher among smokers and is directly related to the number of cigarettes smoked. The mortality ratios reported for both diseases combined are similar to those reported for the U.S. Veterans study.

TABLE 2.—Age-adjusted mortality ratios for current smokers of cigarettes only, by number of cigarettes smoked daily

Cause of death	Cigarettes smoked per day at entrance to study				
	Occasional or never smoked	1-9	10-20	21-39	40+
Bronchitis or emphysema or both (500-502, 527.1).....	1.0	4.6	10.0	11.8	18.2
Bronchitis with or without emphysema (500-502).....	1.0	3.6	4.5	4.6	8.3
Emphysema (527.1).....	1.0	5.3	14.0	17.0	25.3

SOURCE: U.S. Veterans study (44).

TABLE 2A.—Age-specific annual probabilities of death per 100,000¹ person-years, for current smokers of cigarettes only

	Cigarettes smoked per day at entrance to study					All quantities
	Occasional or never smoked	1-9	10-20	21-39	40+	
Chronic bronchitis and/or emphysema:						
Age 55 to 64.....	2	12	32	30	39	29
Age 65 to 74.....	10	66	100	141	322	113
Chronic bronchitis:						
Age 55 to 64.....	1	5	5	5	5	4
Age 65 to 74.....	5	15	22	30	46	23
Emphysema without bronchitis:						
Age 55 to 64.....	1	7	27	26	34	25
Age 65 to 74.....	5	52	78	111	276	90

¹ Annual probabilities of death at each single year of age were combined into 10-year age groups by using weights proportional to the distribution of the U.S. male population in 1960. Not shown if less than 50 person-years of observation at any single year of age in the 10-year interval.

SOURCE: U.S. Veterans study (44).

When the two diseases are separated, the ratios for emphysema in the Canadian study are similar to those for chronic bronchitis in the U.S. study, and the ratios for chronic bronchitis are similar to those attributed to emphysema in the United States. This illustrates the

problems of definition and one of the difficulties of direct comparison between studies, especially when different countries are involved.

TABLE 3.—*Age-adjusted mortality ratios for smokers of cigarettes only by number of cigarettes smoked daily*

Cause of death	Cigarettes smoked per day at entrance to study			
	Non-smokers	1-9	10-20	21+
Bronchitis or emphysema or both.....	1.0	6.1 ¹	10.0 ¹	10.4 ¹
Bronchitis with or without emphysema (500-502).....	1.0	7.0	13.7	14.6
Emphysema (527.1).....	1.0	4.8	6.1	6.9

¹ Calculated from (18).

SOURCE: Canadian Pensioners study (18).

A study among British physicians, the first of the large prospective studies, was started in 1951 with the sending of a short questionnaire to the 59,600 registered physicians then resident in the United Kingdom. Usable replies were received from 34,455 men and 6,192 women. Ten years of observation of mortality in relation to smoking was recently reported for this population by Doll and Hill (29, 30). Their findings on mortality from chronic bronchitis as related to smoking included emphysema and are given in table 4. Only the standardized death rates were presented in the report but the mortality ratios have been calculated from them to offer an easier comparison with the other two studies. Again, it is clear that mortality from these combined diseases (no attempt was made to differentiate them in the published report) is strongly and directly related to the amount of cigarette smoking.

TABLE 4.—*Standardized death rates, per 100,000 population, for bronchitis and emphysema for male smokers of cigarettes only, by number of cigarettes smoked daily*

Cause of death	Cigarettes smoked per day at entrance to study			
	Never smoked	1-14	15-24	25+
Bronchitis (including emphysema—502, 527.1).....	5	34	64	106
Mortality ratios.....	1.0	6.8	12.8	21.2

SOURCE: Study of British Physicians (29, 30).

The fourth of the prospective studies is the largest. More than 1 million men and women living in 25 States were enrolled in this investigation in late 1959 and early 1960. A report of the first 4 years of observation was published recently by Hammond (36) and mortality from emphysema and chronic bronchitis as related to smoking is given in table 5. A slight departure from the usual assignment of cause of death should be mentioned. When the cause of death was listed as chronic bronchitis with emphysema, it was combined with emphysema alone. For this reason, the cause of death in table 5 is not quite the same as any of the causes listed in the other tables. Again, it is clear that mortality from these entities is related to smoking for both men and women. This was the only one of the four studies with enough women enrolled to provide meaningful data.

TABLE 5.—*Mortality ratios for deaths due to emphysema and bronchitis with emphysema for cigarette smokers—men and women in 2 age groups†*

Cause of death	Men (age in years)		Women (age in years)	
	45-64	65-79	45-64	65-79
Emphysema and bronchitis with emphysema (502, 527.1) -----	6.5	11.4	4.9	7.5 ¹

† Mortality ratios of nonsmokers in the above categories are 1.00 by definition.

¹ Calculated from (36).

SOURCE: Hammond, E. C. (36).

Before summarizing the data presented from these four investigations, two further points should be made. Excessive mortality was largely confined to cigarette smokers. The mortality ratio for chronic bronchitis and emphysema, for pipe and cigar smokers combined, in the U.S. veterans study, was only 0.99; in the Canadian study it was about 1.6 (based on only nine deaths); in the study of men from 25 States it was 1.37; and among British doctors the standardized death rate was 15 (compared with five among nonsmokers). Whatever may be the relationship of pipe and cigar smoking to chronic bronchitis and emphysema, it is clear that it is substantially less important than the relationship of cigarette smoking.

In two of these studies, stopping cigarette smoking is seen to have an effect on subsequent mortality from chronic bronchitis and emphysema. In the course of the followup of the British physicians (29, 30) it was possible to estimate the number of years a man continued smoking after he had answered the initial questionnaire. For chronic bronchitis the mortality rates at first increased after cessation of smoking and later fell well below the rate for men who continued to smoke. The death rate from chronic bronchitis, per 100,000

ex-smokers of 5 years or more was 37 compared with a rate of 59 for all other smokers. Similarly, in the study of U.S. veterans, the mortality ratio for chronic bronchitis and emphysema was 10.1 for all male current cigarette smokers but only 7.6 for men who had stopped smoking for reasons other than "Doctor's orders."

RETROSPECTIVE STUDIES

Wicken (75) made a study of lung cancer and bronchitis mortality in Northern Ireland. During the 3 years, 1960-62, a total of 1,262 men and 630 women, aged 35 years or more, were certified as having died of bronchitis. For each of these persons a control was selected—the next person in the Register of the same sex and 5-year age group who last resided in the same area and who died of a nonrespiratory illness. Personal interviews with relatives of the decedents were carried out for about 94 percent of the subjects and controls to determine the decedents' smoking habits. In addition, a random sample of about 1,500 households in Northern Ireland was selected and one member of each household was interviewed to obtain details of the age, sex, smoking habits, and other information on all adult members. This information on all adult members was used to define the adult population of Northern Ireland in order to calculate death rates.

Bronchitis mortality for both men and women was associated with smoking and directly related to the number of cigarettes smoked daily, as seen in table 6.

TABLE 6.—Age-standardized death rates per 100,000 population from bronchitis for adults 35 years old and over as related to smoking habits

	Nonsmoker	Number of cigarettes smoked daily			Smoker of—	
		1-10	11-22	23+	Cigarettes, pipes or cigars	Pipes or cigars
Men.....	(124) ¹ 64	(245) 189	(300) 220	(168) 284	(62) 99	(289) 118
Women..	(490) 58	(57) 77	(20) 118	(15) 201	-----	(2) 165

¹ Figures in parentheses show the number of deaths upon which the rates are based.

SOURCE: Wicken study (75).

Using these data, Wicken applied the bronchitis death rates observed among male non-smokers to all the male population of Northern Ireland and estimated that had these rates prevailed, only 45 percent of the male deaths from bronchitis would have occurred.

RÉSUMÉ

Recent data from the four prospective studies and the one retrospective study all reveal, for men, an association between cigarette smok-

ing and mortality from bronchitis and emphysema. All report an increasing gradient of mortality with an increasing amount smoked. This was also true among women although only one prospective study and the retrospective study included enough women to permit calculation of death rates. Mortality was consistently higher among cigarette smokers than among men who smoked pipes or cigars. These are consistent associations that might be expected if there were a causal relation between cigarette smoking and these diseases. In addition, if such a relationship exists, cessation of smoking should be followed by a reduction in mortality. This did occur in the two studies that included information on changes in smoking habits.

These data, then, strongly support the conclusion that cigarette smoking is at least one of the causes of chronic bronchitis and emphysema.

CHRONIC BRONCHOPULMONARY DISEASE MORBIDITY

STUDIES RELATING SMOKING TO RESPIRATORY SYMPTOMS

Most surveys of chronic respiratory disease are confined to the frequency of signs or symptoms of disease. The National Center for Health Statistics, however, in interviews from July 1964 to June 1965, asked about certain chronic conditions including chronic bronchitis and emphysema (72). This was asked in a national sample of 42,000 households containing about 134,000 persons. After answering questions about health for himself and other members of the household, the respondent was asked questions about their smoking habits. A strong relationship was found between smoking habits and the presence of chronic bronchitis or emphysema or both. This is presented in table 7.

TABLE 7.—*Age-adjusted prevalence rates of chronic bronchitis and/or emphysema per 100 persons 17 years and over, by sex, and smoking status—number of cigarettes per day (heaviest amount)*

	Never smoked	Former smokers	Present smokers		
			1-10	11-20	21+
Men.....	1.0	2.5	1.1	2.3	3.3
Women.....	1.2	2.6	1.6	4.0	6.5

SOURCE: National Center for Health Statistics (72, Fig. 5).

In another study of the epidemiology of persistent cough, Wynder (80) and his associates evaluated the smoking habits, occupation, and residence (urban or rural) in a male population comprised of 315 hospital patients in New York, and 315 in California, and of 239 Seventh-Day Adventists living in California who were not hospital patients. Persistent cough was reported from 23 percent of the Adventists (who do not smoke), 45 percent of the New York patients, and 53 percent of the California patients. Coughing was more frequently reported by cigarette smokers than by those who smoked pipes or cigars, as shown in table 8. Inhalers also had a higher rate of persistent cough and the rate of cough increased with smoking in each age group. Wynder found no correlation between urban or rural residence and persistent cough. Analysis of the California group showed a higher rate of persistent cough that was independent of the number of cigarettes smoked.

TABLE 8.—Percent of men with persistent cough as related to smoking habits

	Non-smoker	Pipes/cigars	Cigarettes only			Mixed smoker
			1-10	11-20	20+	
New York patients.....	14	33	45	46	67	51
California patients.....	22	30	45	74	74	66
Seventh-Day Adventists.....	23					

SOURCE: Wynder, E. L. et al. (80).

Deane and her associates (28) studied symptoms in relation to smoking in a group of about 500 outside telephone workers over age 40 working in the San Francisco and Los Angeles areas. Symptoms were reported on a modified version of the British Medical Research Council questionnaire. Regardless of the definition of the respiratory symptom—persistent cough and phlegm, persistent cough, phlegm, and shortness of breath—it was consistently experienced by a greater proportion of those who currently smoked cigarettes than those who did not.

Coates and his coworkers (20) also found among 1,584 postal workers aged 40 or more (all employees of the Detroit Main Post Office), that for every symptom—cough and phlegm, chronic phlegm alone, wheezing, shortness of breath—the prevalence was two to three times greater among moderate (15-24 cigarettes per day) and heavy (25 or more) smokers than among those who did not smoke. These differences in symptom prevalence were observed for both men and women but "chronic bronchitis" was reported more often by men, which Coates ascribes to their being heavier smokers. The prevalence of chronic

cough and phlegm among ex-smokers was no greater than in nonsmokers.

Very few studies have been carried out to estimate the association of morbidity and smoking in young people. Peters and Ferris (60) retrospectively tallied the number of visits to the clinic at the University of Health Services for 1,623 Harvard students and 404 Radcliffe students. Smoking information had been gathered on these students in their freshman and senior years. Smokers made significantly more visits to the clinic in total and for respiratory diseases in particular. There was a positive correlation between years smoked and the number of respiratory disease visits.

In contrast to most studies which select population groups, Huhti (43) studied virtually the entire population, age 40-64, in a commune in western Finland. Although it was a mostly rural population, some industrial workers were included. More than 95 percent of the men and women invited responded to the survey. Questionnaires (based on that of the British Medical Research Council) and medical examinations were completed for 730 men and 890 women. Only 18.7 percent of the men were nonsmokers and 21.6 percent ex-smokers, compared with 86.1 percent nonsmokers and 3.6 percent ex-smokers among women. Prevalence of both cough and phlegm production was significantly higher among smokers than nonsmokers as seen in table 9.

TABLE 9.—Percent of men and women with cough (3 months in the year) and with phlegm (3 months in the year), related to smoking habits

	Cigarettes smoked per day			Non-smokers	Ex-smokers
	1-14	15-24	25+		
Cough:					
Men.....	31.5	40.8	42.4	4.1	8.5
Women.....	10.4	(3 of 7 women smoking 15+ cigarettes/day)		4.5	13.3
Phlegm:					
Men.....	38.0	42.9	42.4	10.7	17.7
Women.....	10.4	(4 of 7 women smoking 15+ cigarettes/day)		5.9	13.3

SOURCE: Huhti, E. (43).

RÉSUMÉ

In all the prevalence studies that have been identified and reviewed, significantly more cigarette smokers consistently reported having symptoms related to chronic respiratory disease. This was true for cough, production of phlegm, wheezing, and shortness of breath. It

was also true when the respondents were asked not about symptoms but about disease, that is, chronic bronchitis and emphysema, and in one instance was reflected in the number of clinic visits for respiratory diseases. Prevalence of these symptoms increased with the amount of cigarettes smoked. It was less among pipe and cigar smokers, and ex-cigarette smokers among whom the prevalence, in some reports, approached that of nonsmokers.

STUDIES RELATING SMOKING TO PULMONARY FUNCTION

Many of the surveys outlined in the previous section on respiratory symptoms also included lung function tests as part of the examination. Huhti (43), for example, in his Finnish study took chest X-rays and collected information on vital capacity, 1-second forced expiratory volume (FEV_{1.0}) and peak expiratory flow (PEF) as shown in table 10.

TABLE 10¹.—Mean values of lung function tests among men and women by smoking habits

	Cigarettes smoked per day			Non-smokers	Ex-smokers
	1-14	15-24	25+		
FEV _{1.0} (liters):					
Men.....	3. 17	3. 30	3. 08	3. 46	3. 39
Women.....	2. 74	(²)	(²)	2. 42	2. 32
FVC (liters):					
Men.....	4. 40	4. 51	4. 26	4. 40	4. 51
Women.....	3. 53	(²)	(²)	3. 18	3. 19
PEF (c.c./sec.):					
Men.....	518	537	517	569	551
Women.....	431	(²)	(²)	410	403

¹ Although this table presents data for all ages combined, the same differences were apparent in each 5-year age grouping.

² Only 7 women smoked 15 or more cigarettes per day.

SOURCE: Huhti, E. (43).

Among men the FEV_{1.0} value was lower for smokers than nonsmokers. The PEF value was slightly lower, but the vital capacity was unrelated to smoking. In this study none of the values seemed to be clearly related to the number of cigarettes smoked. Among the relatively small number of female smokers in this study, most of whom smoked between one and 14 cigarettes per day, almost all the lung function values were better than in the female nonsmokers. Female smokers were slightly taller in height and slightly lighter in weight than female nonsmokers, which may account for this finding. However, female ex-smokers had slightly reduced FEV_{1.0} and PEF when compared

with female nonsmokers, similar to the relationship noted between male ex-smokers and male nonsmokers.

Coates (20) observed no relation between smoking habits and vital capacity or $FEV_{1.0}$. He did find, however, that the ratio of $FEV_{1.0}/VC$ was significantly lower among heavy smokers (25 or more cigarettes per day) than nonsmokers. This was found for all but the oldest group of workers, but here the number of subjects was small.

Peters and Ferris (59) asked 133 Harvard College seniors to complete a questionnaire on respiratory symptoms and to perform some sample tests of pulmonary functions. Of these, 124 responded. When classified by smoking history, the smokers were found to record more frequent cough, phlegm production, breathlessness, and wheezing with or apart from colds. There was no difference in vital capacity between smokers and nonsmokers. Although the forced expiratory volume in 1 second ($FEV_{1.0}$) was less for heavy smokers than nonsmokers, this was not significant by itself. As a ratio of vital capacity this did show a significant decrease. The air flow rate using the Wright peak-flow meter and other flow rates determined from tracings of the Stead-Wells spirometer ($FR_{75\%}$, $FR_{50\%}$, $FR_{25\%}$, $FR_{10\%}$) did show statistically significant reductions in heavy smokers as compared to nonsmokers. These data show that relatively young cigarette smokers have some impairments of ventilatory function, in turn suggesting the possibility of a rather immediate effect of cigarette smoking on respiratory symptoms and ventilatory function.

A series of experiments has been done by Krumholz and his associates (49, 50, 51) to evaluate cardiopulmonary function in young apparently healthy persons. The first experiment (49) involved 18 house staff physicians ranging in age from 24 to 37 years. Nine had smoked at least one pack of cigarettes a day for the preceding 5 years and nine had not smoked for at least the same time period. Extensive pulmonary function studies were done at rest and after exercise. The smokers were found to have a greater oxygen debt after exercise, decreased diffusing capacity at rest and with exercise, and decreased total lung capacity and vital capacity.

In the second Krumholz experiment (50) 10 young staff physicians, all of whom had smoked at least one pack a day for 5 years, were given pulmonary function tests immediately after and again 3 weeks after abstinence from smoking. Six physicians refrained from smoking for 6 weeks and were tested again. After 6 weeks of no smoking, expiratory peak flow and pulmonary diffusing capacity were significantly increased. Heart rate and oxygen debt after exercise were decreased. After 6 weeks functional residual capacity was decreased and inspiratory reserve volume and maximal voluntary ventilation were increased.