TABLE 17.—Lung cancer mortality ratios for cigar and pipe smokers by amount smoked

Smoking type	Mortality ratio	Number of deaths
Nonsmoker	1.00	78
Cigar smokers:		
< 5 cigars per day	1.14	12
5 to 8 cigars per day	2.64	11
> 8 cigars per day	2.07	2
Pipe smokers:		
< 5 pipefuls per day	.77	2
5 to 19 pipefuls per day	2.20	12
> 19 pipefuls per day	2.47	3
Cigar and pipe:		
8 or less cigars, 19 or less pipefuls	1.62	18
> 8 cigars, > 19 pipefuls	2.19	2

SOURCE: Kahn, H.A. (*69*)

Abelin and Gsell (*1*) is of particular interest. The smoking habits of 118 male patients with cancer of the lung from a rural area of Switzerland were compared with those reported in a survey of all male inhabitants of a town in the same region. About 20 percent of the population of this area were regular cigar smokers, the most popular cigar being the Stuempen, a small Swiss-made machine-manufactured cigar cut at both ends with an average weight of 4.5 g. In this investigation, cigar smokers experienced a risk of developing lung cancer that was similar to the risk of cigarette smokers. A dose-response relationship was demonstrated for inhalation and amount smoked. These data suggest that the heavy smoking of certain cigars may result in a risk of lung cancer that is similar to that experienced by cigarette smokers.

Sanderud (*106*) examined histologic sections from the bronchial tree of 100 male autopsy cases for the presence of squamous epithelial metaplasia. In this study, 39 percent of the population were nonsmokers, 20 percent were pipe smokers, and 38 percent smoked cigarettes. A total of 80 percent of the pipe smokers and cigarette smokers demonstrated squamous metaplasia of the bronchial tree, whereas only

TABLE 18.—Relative risk of lung cancer for men, comparing cigar, pipe, and cigarette smokers with nonsmokers. A summary of retrospective studies

Author, reference	Number	Relative risk ratio and percentage of cases and controls by type of smoking						
			Non-smoker	Cigar only	Pipe only	Total pipe and cigar	Cigarette only	Mixed
Levin (*80*):		Relative risk	1.0	0.7	0.8	....	2.1	....
Cases	236	Percent cases	15	11	14	....	66	....
Controls	481	Percent controls	22	23	25	....	44	....
Schrek (*110*):		Relative risk	1.0	.6	.7	....	1.7	....
Cases	82	Percent cases	15	4	5	....	61	....
Controls	522	Percent controls	22	23	11	....	59	....
Wynder and Graham (*140*):		Relative risk	1.0	5.1	3.6	....	15.7	....
Cases	605	Percent cases	1	4	4	....	91	....
Controls	780	Percent controls	15	8	12	....	65	....
Doll and Hill (*86*):		Relative risk	1.0	....	5.1	....	9.6	....
Cases	1,357	Percent cases	.5	....	4	....	74	....
Controls	1,357	Percent controls	5	....	7	....	69	....
Koulumies (*77*):		Relative risk	1.0	....	9.6	....	29.3	....
Cases	812	Percent cases	.6	....	2	....	77	....
Controls	300	Percent controls	18	....	6	....	76	....
Sadowsky (*105*):		Relative risk	1.0	2.4	1.4	....	3.7	5.6
Cases	477	Percent cases	4	2	3	....	57	31
Controls	615	Percent controls	13	3	7	....	53	19
Wynder and Cornfield (*139*):		Relative risk	1.0	2.5	4.0	....	8.5	....
Cases	63	Percent cases	4	13	6	....	77	....
Controls	133	Percent controls	21	27	8	....	45	....
Randig (*100*):		Relative risk	1.0	5.3	5.0	....	5.0	....
Cases	415	Percent cases	1	21	11	....	67	....
Controls	381	Percent controls	6	19	11	....	64	....
Mills and Porter (*86*):		Relative risk	1.0	....	....	6.0	5.4	....
Cases	444	Percent cases	7	....	....	37	55	....
Controls	430	Percent controls	31	....	....	26	43	....
Mills and Porter (*87*):		Relative risk	1.0	....	....	2.8	4.5	....
Cases	484	Percent cases	8	....	....	13	78	....
Controls	1,588	Percent controls	28	....	....	16	57	....

54 percent of the nonsmokers had this abnormality. Knudtson (*76*) also studied histologic changes.

Auerbach, et al. (*8*) examined 36,340 histologic sections obtained from 1,522 white adults for various epithelial lesions including:

TABLE 18.—Relative risk of lung cancer for men, comparing cigar, pipe, and cigarette smokers with nonsmokers. A summary of retrospective studies–continued

Author, reference	Number		Relative risk ratio and percentage of cases and controls by type of smoking					
			Non-smoker	Cigar only	Pipe only	Total pipe and cigar	Cigarette only	Mixed
Schwartz and Denoix (*111*):		Relative risk	1.0	....	4.7	....	13.5	....
Cases	430	Percent cases	1	....	6	....	96	....
Controls	430	Percent controls	11	....	14	....	78	....
Stocks (*123*):		Relative risk	1.0	....	3.1	....	5.0	....
Cases	2,101	Percent cases	2	....	9	....	89	....
Controls	5,960	Percent controls	9	....	13	....	78	....
Lombard and Snegireff (*81*):		Relative risk	1.0	....	....	1.7	8.1	....
Cases	500	Percent cases	2	....	....	4	95	....
Controls	1,839	Percent controls	10	....	....	15	75	....
Pernu (*99*):		Relative risk	1.0	....	4.2	....	9.2	11.1
Cases	1,477	Percent cases	7	....	4	....	77	13
Controls	713	Percent controls	39	....	5	....	50	7
Wicken (*135*):		Relative risk	1.0	....	....	2.2	4.3	4.2
Cases	803	Percent cases	4	....	....	10	78	7
Controls	803	Percent controls	14	....	....	16	64	6
Abelin and Gsell (1):		Relative risk	1.0	3.4	4.5	....	5.7	
Cases	118	Percent cases	2	28	7	....	....	24
Controls	524	Percent controls	35	19	6	....	....	10
Wynder (*144*):		Relative risk	1.0	....	....	2.0	12.4	....
Cases	210	Percent cases	3	....	....	5	92	....
Controls	420	Percent controls	21	....	....	15	47	....

presence or absence of ciliated cells, thickness or number of cell rows, atypical nuclei, and the proportion of cells of various types. The pathologic findings in the bronchial epithelium of pipe and cigar smokers were compared to those found in nonsmokers and cigarette smokers. Pipe and cigar smokers had abnormalities that were intermediate between those of nonsmokers and cigarette smokers, although cigar smokers had pathologic changes that in some categories approached the changes seen in cigarette smokers.

Tumorigenic Activity

Several experimental investigations have been conducted to examine the relative tumorigenic activity of tobacco smoke condensates obtained from cigarettes, cigars, and pipes. Most of these studies were standardized in an attempt to make the results of the cigar and pipe

experiments more directly comparable with the cigarette data, and most used the shaved skin of mice for the application of tar. Tars from cigars, pipes, and cigarettes were usually applied on an equal weight basis so that qualitative differences in the tars could be determined. In several experiments, the nicotine was extracted from the pipe and cigar condensates in an attempt to reduce the acute toxic effects that resulted in animals from the high concentrations of nicotine frequently found in these products.

Wynder and Wright (*146*) examined the differences in tumorigenic activity of pipe and cigarette condensates. Tars were obtained by the smoking of a popular brand of king-size cigarettes and from the same cigarette tobacco smoked in 12 standard-grade briar bowl pipes. Both the cigarettes and pipes were puffed three times a minute with a 2-second puff and a 35-ml volume. Both the cigarettes and pipes attained similar maximum combustion zone temperatures; however, the use of cigarette tobacco in the pipe resulted in a combustion chamber temperature that averaged about 150° centrigrade higher than temperatures achieved when pipe tobacco was used. Chemical fractionation was accomplished and equal concentrations of the neutral fraction were applied in three weekly applications to the shaved skin of CAF_1 and Swiss mice. The results indicate that neutral tar obtained from cigarette tobacco smoked in pipes is more active than that obtained in the usual manner from cigarettes. About twice as many cancers were obtained in both the CAF_1 and the Swiss mice, and the latent period was about 2 months shorter.

Extending these data, Croninger, et al. (*27*) examined the biologic activity of tars obtained from cigars, pipes, and cigarettes. Each form of tobacco was smoked as it was manufactured in a manner to simulate human smoking or to maintain tobacco combustion. The whole tar was applied in dilutions of one-to-one and one-to-two with acetone to the shaved backs of female CAF_1 and female Swiss mice using three applications each week for the life span of the animal. The nicotine was extracted from the pipe and cigar condensates to reduce the acute toxicity of the solutions. In the Swiss mice, pipe, cigar, and cigarette tars produced both benign and malignant tumors. The incidence rates of malignant tumors given as percents were: 44, 41, and 37, respectively. These results suggested a somewhat higher degree of carcinogenic activity for cigar and pipe tars than for cigarette tar.

Similar results were reported by Kensler (*72*), who applied condensates obtained from cigars and cigarettes to the shaved skin of mice. The incidence of papillomas produced by cigar smoke concentrate was no different from that produced by the cigarette smoke condensate. Similarly, there was no difference between cigar and cigarette smoke condensates when carcinoma incidences were compared.

Homburger, et al. (*62*) prepared tars from cigar, pipe, and cigarette tobaccos that were smoked in the form of cigarettes. In this way, all

tobaccos were smoked in an identical manner and uniform combustion temperatures were achieved. Because of this standardization, differences in tumor yield could be attributed to tobacco blend and not to the manner in which the tars were prepared. The whole tars were diluted one-to-one with acetone and applied to the shaved skin of CAF_1 mice three times a week for the life span of the test animal. Skin cancers were produced more quickly with pipe and cigar smoke condensates than with cigarette smoke condensates. This suggests that the smoking of pipe and cigar tobaccos in the form of cigarettes does not alter the condensates to any significant degree. Davies and Day (*29*) and Roe, et al. (*103*) conducted other tumorigenic studies.

These experimental data suggest that cigar and pipe tobacco condensates have a carcinogenic potential that is comparable to cigarette condensates. This is supported by human epidemiological data for those sites exposed equally to the smoke of cigars, pipes, and cigarettes. The partially alkaline smoke derived from pipes and cigars is generally not inhaled, and as a result there appears to be a lower level of exposure of the lungs and other systems to the harmful properties of pipe and cigar smoke than occurs with cigarette smoking. It is anticipated that modifications in pipe tobacco or cigars which would result in a product that was more readily inhalable would eventually result in elevated mortality from cancer of the lung, bronchitis and emphysema, arteriosclerotic cardiovascular diseases, and the other conditions which have been clearly associated with cigarette smoking.

Cardiovascular Diseases

Pipe and cigar smokers experience only a small increase in mortality from coronary heart disease above the rates of nonsmokers. Cigarette smokers have higher death rates from cerebrovascular disease than nonsmokers, whereas pipe and cigar smokers have cerebrovascular death rates that are only slightly above the rates of nonsmokers. Table 19 summarizes the major prospective epidemiological investigations that examined the association of smoking in various forms with total cardiovascular diseases, coronary heart disease, with cerebrovascular disease. Doll and Hill (*33*), Best (*11*), and Kahn (*69*) examined dose-response relationships for pipe and cigar smokers and reported a slight increase in mortality from coronary heart disease with an increase in the number of cigars or pipefuls smoked.

Other prospective epidemiological studies have also examined the relationship of smoking in various forms to coronary heart disease and related risk factors. Jenkins, et al. (*66*), in the Western Collaborative Group Study of coronary heart disease (CHD), reported an incidence of coronary heart disease in men aged 50 to 59 who were pipe and cigar smokers that was intermediate between the rates seen in cigarette smokers and nonsmokers. No increase in incidence of coronary heart

TABLE 19.—Mortality ratios for cardiovascular deaths in male cigar and pipe smokers. A summary of prospective epidemiological studies

Author, reference	Category	Type of smoking					
		Non-smoker	Cigar only	Pipe only	Total pipe and cigar	Cigarette only	Mixed
Hammond and Horn (*52*).	Cardiovascular total.	1.00	1.26	1.07	....	1.57	....
	Coronary.....	1.00	1.28	1.03	....	1.70	....
	Cerebrovascular....	1.00	1.31	1.23	....	1.30	....
Doll and Hill (*38*).	Cardiovascular total.	1.00	....	....	.81	1.38	.81
	Coronary.....	1.00	....	....	1.03	1.62	1.28
	Cerebrovascular....	1.00	....	....	1.15	1.34	1.21
Best (*11*).	Cardiovascular total.	1.00	1.14	.95	....	1.52	....
	Coronary.....	1.00	.99	1.00	....	1.60	....
	Cerebrovascular....	1.00	1.28	.85	....	.88	....
Hammond[1] (*50*).	Cardiovascular total.	1.00	....	....	1.06	1.90	....
	Coronary.....	1.00	1.35	1.19	....	1.09	1.41
	Cerebrovascular....	1.00	....	....	1.09	1.41	1.40
Kahn (*69*).	Cardiovascular total.	1.00	1.05	1.06	1.05	1.75	....
	Coronary.....	1.00	1.04	1.08	1.05	1.74	....
	Cerebrovascular....	1.00	1.08	1.09	1.06	1.52	....

[1]Mortality ratios for ages 55 to 64 only are presented.

disease was seen among the pipe and cigar smokers in the younger age groups. Shapiro, et al. (*115*), in a study of the health insurance plan (HIP) population, reported incidence rates for myocardial infarction (MI), angina pectoris, and possible MI, in pipe and cigar smokers that were similar to the incidence rates seen in cigarette smokers. These rates were considerably higher than those of nonsmokers. Data from the Pooling Project (*64*) suggested that the incidence of CHD deaths, sudden death, and the first major coronary event in pipe and cigar smokers was intermediate between the incidence experienced by cigarette smokers and nonsmokers. In contrast to these studies, Doyle, et al. (*39*) reported no increase in CHD deaths, myocardial infarction, or angina pectoris in pipe and cigar smokers over the rates of nonsmokers in the Framingham study.

The retrospective studies of Mills and Porter (*85*), Villiger and Heyden-Stucky (*133*), Schimmler, et al. (*109*), and Hood, et al. (*63*) contained data suggesting that pipe and cigar smokers experience mortality rates from coronary heart disease that are essentially similar

to those experienced by cigarette smokers. The retrospective study of Spain and Nathan (*120*) reported lower rates of coronary heart disease for pipe and cigar smokers than were found in nonsmokers.

Van Buchem (*132*) and Dawber, et al. (*30, 31*) examined serum cholesterol levels in groups of individuals classified according to smoking habits. In these two studies, pipe and cigar smokers had serum cholesterol levels that were nearly identical with the levels found in nonsmokers.

Tibblin (*125*) and Dawber, et al. (*30, 31*) investigated the effect of smoking on blood pressure. The proportion of smokers decreased in groups with higher blood pressures, although this was not as dramatic for pipe and cigar smokers as it was for cigarette smokers. Kesteloot and Van Houte (*75*) found that pipe and cigar smokers had slightly lower blood pressures than nonsmokers, in contrast to cigarette smokers who had minimally elevated blood pressures in comparison to nonsmokers.

Chronic Obstructive Pulmonary Disease

Chronic bronchitis and pulmonary emphysema account for most of the morbidity and mortality from chronic respiratory disease in the United States. The relationship between smoking pipes and cigars and these diseases is summarized in this section and in Table 20.

In a retrospective study of 1,189 males and matched controls in Northern Ireland, Wicken (*135*) investigated smoking in various forms and mortality from bronchitis. The relative risk ratios compared to nonsmokers for mortality from chronic bronchitis were 1.98 for all smokers, 1.55 for pipe and cigar smokers, 2.25 for cigarette smokers, and 1.49 for mixed smokers.

From a review of these prospective and retrospective studies, it appears that pipe and cigar smokers experience mortality rates from bronchitis and emphysema that are higher than the rates of nonsmokers. Although these mortality rates approach those of cigarette smokers, in most instances they are intermediate between the rates of cigarette smokers and nonsmokers.

Pipe and cigar smokers have significantly more respiratory symptoms and illnesses than nonsmokers. Those studies which contain data on pipe and cigar smoking as related to respiratory symptoms are summarized in Table 21.

Haenszel and Hougen (*48*) showed an increased prevalence of persistent cough and phlegm in pipe and cigar smokers compared to nonsmokers and were able to show that the prevalence increased with increasing amount smoked.

Only a few studies have examined pulmonary function in pipe and cigar smokers. There appears to be little difference in pulmonary

TABLE 20.—Mortality ratios for chronic obstructive pulmonary deaths (COPD) in male cigar and pipe smokers. A summary of prospective epidemiological studies

Author, reference	Category	Type of smoking					
		Non-smoker	Cigar only	Pipe only	Total pipe and cigar	Cigarette only	Mixed
Hammond and Horn (*52*).	COPD total	1.00	1.29	1.77	....	2.85	....
	Exmphsema	....	....	....	....	....	....
	Bronchitis	....	....	....	....	....	....
Doll and Hill (*34,35,38*).	COPD total	1.00	....	....	9.33	24.67	11.33
	Emphysema	....	....	....	....	....	....
	Bronchitis	1.00	....	....	4.00	7.00	6.67
Best (*11*).	COPD total	....	....	....	....	....	....
	Emphysema	1.00	3.33	.75	....	5.85	....
	Bronchitis	1.00	3.57	2.11	....	11.42	....
Hammond (*50*).	COPD total	....	....	....	....	....	....
	Emphysema	1.00	....	....	1.37	6.55[1]	....
	Bronchitis	....	....	....	....	....	....
Kahn (*69*).	COPD total	1.00	.79	2.36	.99	10.08	....
	Emphysema	1.00	1.24	2.13	1.31	14.17	....
	Bronchitis	1.00	1.17	1.28	1.17	4.49	....

[1]Only mortality ratios for ages 55 to 64 are presented.

function values for pipe and cigar smokers as compared to nonsmokers (Table 22).

Naeye (*88*) conducted an autopsy study on 322 Appalachian coal workers who were classified according to the type of coal mined and tobacco usage. Emphysema was slightly greater in cigarette smokers, as were anatomic evidences of chronic bronchitis and bronchiolitis. Those changes found in pipe and cigar smokers were intermediate between those of cigarette-smoking miners and nonsmoking miners.

Changes in pulmonary histology in relation to smoking habits and age were examined by Auerbach, et al. (*6, 10*). Fibrosis, alveolar rupture, thickening of the walls of small arteries, and thickening of the walls of the pulmonary arterioles were found to be highly related to the smoking habits of the 1,340 male subjects examined. The 91 pipe and cigar smokers over the age of 60 were found to have somewhat more alveolar rupture than the men of the same age distribution who never smoked regularly. However, pipe and cigar smokers as a group had far less rupture than cigarette smokers. The same relations as described above were found for fibrosis, thickening of the walls of the arterioles and small arteries, and padlike attachments to the alveolar septums.

TABLE 21.—Prevalence of respiratory symptoms and illness by type of smoking

Author, reference	Number and type of population	Illness	Percent prevalence			
			Non-smoker	Total pipe and cigar	Cigarette only	Mixed
Boake (*12*).	Parents of 59 families.	Cough.	32	32	48	....
		Sputum production.	24	15	20	....
		Chest illness.	5	4	5	....
Edwards (*42*).	1,737 male outpatients.	Chronic bronchitis.	17	19[1]	31	14
Ashford (*5*).	4,014 male workers in 3 Scottish collieries.	Bronchitis.	10	35[1]	21	37
		Pneumoconiosis.	11	34[1]	14	2
Bower (*14*).	95 male bank employees.	Cough.	0	0	29	....
		Sputum production.	8	15	33	....
		Wheeze.	8	31	33	....
		Chest illness.	15	54	40	....
Wynder (*143*).	315 male patients in New York and 315 male patients in California.	Cough (New York).	14	33	56	51
		Cough (California).	22	30	67	66
		Influenza (New York).	11	21	24	....
		Influenza (California).	28	24	31	....
		Chest illness (New York).	9	10	12	....
		Chest illness (California).	7	6	11	....
Densen (*32*).	5,287 male postal and 7,213 male transit workers in New York City.	Persistent cough.	7	11	25	....
		Persistent sputum production.	11	16	26	....
		Dyspnea.	16	19	26	....
		Wheeze.	14	21	32	....
		Chest illness.	13	16	18	....
Cederlof (*23*).	4,379 twin pairs, all U.S. veterans.	Cough.	4	7	17	....
		Prolonged cough.	2	4	11	....
		Bronchitis.	2	3	10	....
Rimington (*102*).	41,729 male volunteers.	Chronic bronchitis.	5	9[1]	17	....

Tobacco smoke has been shown experimentally to have a ciliostatic

TABLE 21.—Prevalence of respiratory symptoms and illness by type of smoking–continued

Author, reference	Number and type of population	Illness	Percent prevalence			
			Non-smoker	Total pipe and cigar	Cigarette only	Mixed
Comstock (*24*).	670 male telephone employees.	Persistent cough.	10	16	41	....
		Persistent sputum	13	20	42	....
		Dyspnea.	33	39	44	....
		Chest illness in past 3 yrs.	14	18	20	....
Lefcoe and Wonnacott (*79*).	310 male physicians in London, Ontario.	Chronic respiratory disease.	9	18	44	....
		Chronic bronchitis.	1	12	34	....
		Obstructive lung disease.	1	3	4	....
		Asthma.	7	3	6	....
		Rhonchi.	0	3	9	....
Haenszel and Hougen (*48*).	6,712 Norwegian males and 3,887 siblings who emigrated.	Persistent cough and phlegm, age 35-54.	3.0	8.7	14.8	14.5
		Persistent cough and phlegm, age 55–74.	3.7	7.2	15.0	14.3
		Chronic bronchitis, age 35–54.	0.4	1.1	1.9	1.3
		Chronic bronchitis, age 55–74.	1.3	1.6	3.7	3.5

[1]Figures for pipe only.

effect on the respiratory epithelium. The interval between puffs, the amount of volatile and particulate compounds in the smoke, and the exposure volume have been shown to influence the toxic effect of tobacco smoke. Dalhamn and Rylander (*28*) exposed the upper trachea of anesthetized cats to the smoke of cigarettes and cigars, observing the effect on ciliary activity through an incident-light microscope. A chemical analysis of the gas and particulate phases revealed that the cigar smoke was more alkaline and, in general, contained higher concentrations of isoprene, acetone, acetonitrile, toluene, and total particulate matter compared to cigarette smoke. The average number of puffs required to arrest ciliary activity was found to be 73 for the cigarette smoke and 114 for the cigar smoke. The difference is statistically significant ($P < 0.01$). Of the two smokes, the smoke with the highest concentration of volatile compounds was found to be the least ciliostatic. This suggests that the degree of ciliotoxicity of a

TABLE 22.—Pulmonary function values for cigar and pipe smokers as compared to nonsmokers

Author, reference	Number and type of population	Function	Type of smoking			
			Non-smoker	Total pipe and cigar	Cigarette only	Mixed
Ashford (5).	4,014 male workers in 3 Scottish collieries.	$FEV_{1.0}$	3.39	2.59[1]	3.14	2.62
Goldsmith, et al. (47).	3,311 active or retired longshoremen.	Puffmeter	313.63	299.26	303.44	....
		$FEV_{1.0}$	2.99	2.80	2.91	....
		TVC	3.87	3.68	3.88	....
Comstock (24).	670 male telephone employees.	$FEV_{1.0}$	3.12	3.26	2.82	....
Lefcoe and Wonnacott (79).	310 male physicians in London, Ontario.	$FEV_{1.0}$	3.39	3.17	3.11	....
		MMFR liters per second	4.09	4.17	3.64	....

[1]Figures for pipe only.

smoke is not necessarily correlated to the level of one or several of the substances found in the smoke. Passey, et al. (*95*, *96*, *97*) studied smoke effects in rats.

Gastrointestinal Disorders

Cigar and pipe smokers experience higher death rates from peptic ulcer disease than nonsmokers. These rates are higher for gastric ulcers than for duodenal ulcers but are somewhat less than those rates experienced by cigarette smokers. Retrospective or cross-sectional studies by Trowell (*129*), Allibone and Flint (*3*), Doll, et al. (*37*), and Edwards, et al. (*42*) contain data on ulcer disease in pipe smokers as well as cigarette smokers, but no association was found between pipe smoking and ulcer disease in these investigations.

Snuff and Chewing Tobacco

In the United States most of the tobacco consumed is used in pipes, cigars, or cigarettes, forms that involve combustion. Nicotine and other substances can be absorbed through the oral mucosa, however, and so tobacco can also be chewed, inhaled into the nose, or retained between the cheek and gum.

A variety of forms of tobacco are designed for noncombustive use (*141*). Plug tobacco contains Burley, cigar, and Virginia tobaccos sweetened with honey, sugars, molasses, syrups, and licorice, pressed into flattened blocks and then wrapped with natural leaf. Scrap chewing tobacco is made from fermented cigar leaf tobacco. Some brands are only lightly sweetened, whereas others carry large amounts of sugars, syrups, licorice, and other flavoring materials. The treated tobacco is not compressed, but is packaged as loose pieces of cut strips. In some countries, chewing tobacco is made from tar-like material extracted by boiling the green leaves in water. This extract is mixed with slaked lime or wood ashes. When dipped into this mixture, cured leaf absorbs it. These materials are then twisted into strands and allowed to dry. In India, betel nut may be mixed with tobacco leaf to make a chewing tobacco.

Dark air-cured and fire-cured tobaccos are powdered, flavored, and variously packaged to make snuff. The consumer places the snuff between the lower lip and gum, inhales a pinch into the nostril, or dips a moistened brush into the snuff and places the brush between the cheek and gum.

Prevalence of Snuff Use and Tobacco Chewing

Only a small percentage of the United States population chews tobacco (Table 2), and an even smaller percentage uses snuff (*91*, *92*). Use of these products is more frequent in males than in females, and usage is relatively stable.

The combination of the low prevalence of snuff use and tobacco chewing and the low incidence of oral cancer in the U.S. makes it difficult to accumulate the large numbers of subjects necessary for an adequate epidemiologic study. Many of those who now use snuff or chew tobacco are either current or former smokers and, therefore, are likely to obscure an independent effect of snuff or chewing tobacco. Finally, such use involves a very small percentage of the population ethnically, geographically, and culturally different from the general population, which makes it difficult to compare incidence rates with the general population.

Because of these problems, many of the studies on tobacco chewing have been done in Asia, where the prevalence of both oral cancer and tobacco chewing is higher. The validity of applying those results to the United States is questionable, however, because of differences in the type of tobacco chewed, nutritional status, and social habits.

Benign Oral Lesions and Oral Cancer

A population of 15,000 snuff users, 75 percent female, from a large clinic in the southern U.S., was examined by Smith, et al. (*117*) for oral lesions. In most patients no mucosal abnormalities were found, even in the areas of the mouth where the tobacco quid was usually held. Only

1,751 (11.7 percent) demonstrated any mucosal change, and only 157 had lesions suspicious enough to biopsy. The biopsies showed early epithelial changes, such as atrophy, but none of the biopsies showed changes consistent with dyskeratosis or malignancy. Of the 1,751 patients who showed some tissue change by visual examination and had cytologic examinations performed, 1,502 had normal findings, 12 had unsatisfactory smears, and 237 had benign hyperkeratosis. Seventy-five percent of the subjects were followed with repeated cytologic smears at 6-month intervals for 5 1/2 years, and none showed any mucosal changes different from the original testing. The conclusion was that snuff is not a risk factor for oral cancer and is not associated with an excess incidence of other oral lesions.

Roed-Petersen and Pindborg (*103a*), who studied 450 Danish patients with oral leukoplakias, of whom 32 used snuff, were unable to show any difference between snuff-associated leukoplakias and other leukoplakias in degree of dysplasia observed histologically or in malignant development.

In contrast to these negative studies, a number of studies from Asia have found an association between tobacco chewing and oral lesions, but, again, questions of application to an American population arise. Mehta, et al. (*84*), conducted a house-to-house survey of 101,761 villagers in the Poona district of India and found a prevalence of leukoplakia of 1.18 percent in male chewers of tobacco, and 1.84 percent in female chewers. Nonchewers had rates of 0.05 percent for males and 0.04 percent for females. Smokers and those with mixed habits had rates higher than persons who just chewed tobacco. Smith, et al. (*118*) found an increased prevalence of leukoplakia in tobacco chewers compared to nonchewers among 57,518 industrial workers of Gujarat, but none of the tobacco-chewing subjects had developed oral cancer during a 2-year follow-up (*116*). Mehta, et al. (*84*) also found an increased prevalence of leukoplakia in Bombay policemen, but found that the lesions in tobacco chewers tended to regress, whereas lesions in smokers did not.

Jussawalla and Deshpande (*67*) conducted a retrospective study of 2,005 oral cancer patients and matched controls. They found chewing to be associated with an increased risk of cancer of the anterior two-thirds of the tongue, alveolus, buccal mucosa, hard palate, base of the tongue, tonsil, oropharynx, hypopharynx, and esophagus. The risk was greatest for sites where the bolus was retained for a significant length of time, and the locations of greatest risk were considerably different from the sites affected in smokers. They felt that this was due to the different exposures experienced by smokers and chewers. Soda (*119*) also found an excess risk of oral cancer in chewers with a different distribution of lesion sites between chewers and smokers. Shanta and Krishnamurthi (*114*), Sanghvi, et al. (*107*), and Paymaster (*98*) have also found an association between oral cancer and tobacco habits,

especially the use of "pan" consisting of green leaf in which sliced betel nut, tobacco dust, slaked lime, liquified catechu, and other spices are rolled.

In summary, there does seem to be an association between tobacco chewing and leukoplakia and oral cancer in Asia, but it is not clear that the same risk holds true in the United States due to a difference in the tobacco being chewed and to differences in the nutritional status and other characteristics of the population.

Conclusions

Pipe and cigar smokers in the United States as a group experience overall mortality rates that are slightly higher than those of nonsmokers, but at rates substantially lower than those of cigarette smokers. This appears to be due to the fact that the total exposure to smoke that a pipe or cigar smoker receives from these products is relatively low. The typical cigar smoker smokes fewer than 5 cigars a day and the typical pipe smoker consumes less than 20 pipefuls a day. Most pipe and cigar smokers report that they do not inhale the smoke. Those who do, say they inhale infrequently and only slightly.

As a result, the harmful effects of cigar and pipe smoking appear to be largely limited to those sites which are exposed to the smoke of these products. Mortality rates from cancer of the oral cavity, intrinsic and extrinsic larynx, pharynx, and esophagus are approximately equal in users of cigars, pipes, and cigarettes. Inhalation is evidently not necessary to expose these sites to tobacco smoke, and these sites account for only about 5 percent of the cancer mortality among men.

Coronary heart disease, lung cancer, emphysema, and chronic bronchitis clearly are associated with cigarette smoking; but for cigar and pipe smokers, death rates from these diseases are not greatly elevated above the rates of nonsmokers. These diseases seem to depend on moderate to deep inhalation to bring the smoke into direct contact with the tissue at risk or to allow certain constituents, such as carbon monoxide, to be systematically absorbed through the lungs or to affect the temporal patterns of absorption of other constituents, such as nicotine, that can be absorbed either through the oral mucosa or through the lungs. Evidence from countries where smokers tend to consume more cigars and inhale them to a greater degree than in the United States indicates that rates of lung cancer become elevated to levels approaching those of cigarette smokers.

Data on the chemical constituents of cigar, pipe, and cigarette smoke suggest that the composition of these products is similar. Pipe and cigar smoke, however, tends to be more alkaline than cigarette smoke, and fermented tobaccos commonly used in pipes and cigars contain less reducing sugars than the rapidly dried varieties commonly used in cigarettes.

Experimental evidence suggests little difference between the tumorigenic activities of tars obtained from cigar or cigarette tobaccos. Malignant skin tumors appear somewhat more rapidly and in larger numbers in animals whose skin has been painted with cigar tars than in those animals painted with cigarette tars.

It must be concluded that some risk exists from smoking cigars and pipes, as currently used in the United States, but for most diseases the risk is small relative to the enormous risk of smoking cigarettes. Nevertheless, changes in patterns of usage that would bring about increased exposure either through increased use of cigars and pipes or increased inhalation of pipe and cigar smoke have the potential of producing risks similar to those now incurred by cigarette smokers.

Tobacco chewing is associated with an increased risk of leukoplakia and oral cancer in Asian populations, but the risk for populations in the United States is not clear. An increased risk of oral leukoplakia associated with snuff use in the U.S. has not been demonstrated.

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14. CONSTITUENTS OF TOBACCO SMOKE.

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