

mouth and pharynx" (48). Since most people who drink large amounts of alcohol regularly are also heavy users of tobacco, it is difficult to identify the relative contribution of these two factors or the role of the nutritional problems often associated with heavy alcohol use.

Additional data have been reported by Moore (62), on patients developing second primary mouth and throat cancers, after having been cured for at least three years prior to development of the cancer. These patients were all asymptomatic for at least three years prior to development of the second cancer. Of 117 patients with adequate smoking histories only 4 of 43 (9 percent) who quit smoking after the first cancer, developed a new primary. On the other hand, 27 of 74 patients (36 percent) who continued to smoke developed a second primary cancer. These data support the important contribution of smoking to the etiology of mouth and throat cancer.

Roth, et al. (73, 74) recently have shown that the dye-binding capacity of DNA of oral epithelial cells is significantly enhanced in cigarette smokers in contrast to nonsmokers, probably reflecting an increase in the DNA content of oral epithelial cells in smokers. This suggests some alteration in the DNA which may be a factor in oral carcinogenesis. Smokers had values of dye-binding capacity intermediate between nonsmokers and 21 patients with proven oral cancer. Those smokers who refrained from smoking for up to nine months showed a significant decrease towards more normal values.

It is clear that people who use tobacco have higher rates of oral cancer than those who do not. Research is needed to identify the dose relationships, to determine whether or not there are dosage thresholds, and to clarify the relationships between dosage, style of tobacco use, and part of the mouth affected.

It seems likely that factors such as alcohol consumption, nutritional problems, and oral hygiene may be interrelated with the tobacco habit in a fairly complex pattern. More research is needed to clarify these relationships.

For patients with oral cancer, and probably for those at a high risk of oral cancer because of other exposures, cessation of tobacco use can make an important contribution to reducing the risk of a new primary cancer.

## CANCER OF THE LARYNX

Cancer of the larynx is mainly a disease of male smokers. Of the 2,629 deaths in 1965, over 88 percent were men. The 1967 report noted that the death rate for cancer of the larynx had not increased significantly since 1950. The incidence rates, however, have shown a steady increase since 1935.

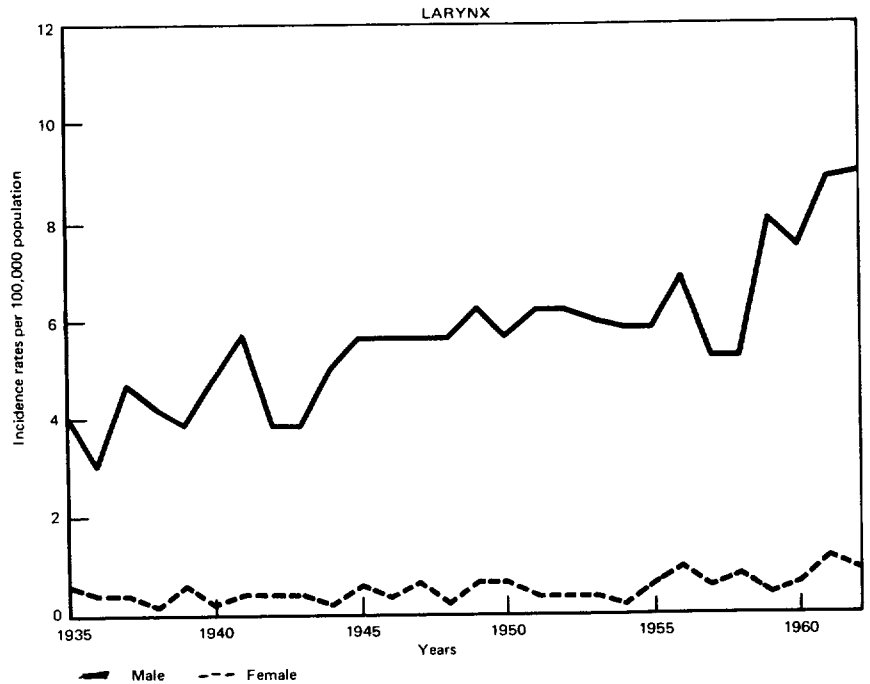


FIGURE 3—Age-adjusted rates of the incidence of cancer of the larynx, for males and females: Connecticut, 1935-1962  
SOURCE: Eisenberg et al. (24).

The American Cancer Society (2) estimates the occurrence of 6,000 new cases of cancer of the larynx in 1968 but only about 2,800 deaths, due to relative curability of this disease if diagnosed early.

Several retrospective studies have again shown the extremely high rate of smokers [98 percent (86), 92 percent (75)] among patients with cancer of the larynx.

### CANCER OF THE ESOPHAGUS

As reported in the 1967 Report (92) the death rates for cancer of the esophagus have increased only slightly in the period 1950-1964. The large scale prospective studies (18, 19, 34, 46) showed mortality ratios up to 11 in heavy cigarette smokers, while pipe and/or cigar smokers had ratios up to 5.

Preliminary data from a prospective study (37) in Japan also indicate an increased frequency of death from cancer of the esophagus among smokers as compared to nonsmokers.

No further information has become available on the relationship of esophageal cancer to alcohol and/or other confounding variables as discussed in the 1967 report.

## CANCER OF THE PANCREAS

The 1967 report implied a relationship between smoking and pancreatic cancer due to the somewhat higher mortality ratios observed in three of the large scale prospective epidemiologic studies.

The American Cancer Society estimates that deaths due to cancer of the pancreas will total 18,000 in 1968 with a male/female ratio of approximately 3:2. The overall death rate for cancer of the pancreas has shown a steady rise; from 7.2 to 8.4 in males (+17 percent) and 4.4 to 4.9 (+11 percent) in females, for the time period 1953-55 to 1963-65 (2). The incidence rates have increased almost 50 percent in males since 1935, with no apparent increase for females.

In the past year, preliminary evidence from two retrospective studies (43, 102) has shown that only 10 percent of the patients with cancer of the pancreas are nonsmokers. The risk of developing cancer of the pancreas appears to increase in proportion to the amount smoked.

Preliminary data from a prospective study (37) in Japan also shows a significantly higher frequency of deaths from pancreatic cancer among smokers as compared to nonsmokers.

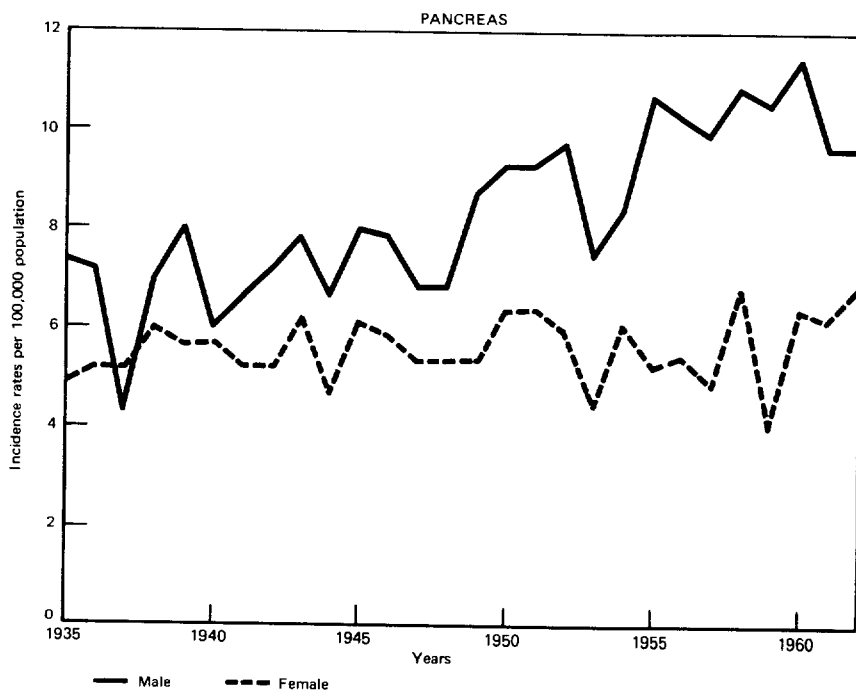


FIGURE 4—Age-adjusted rates of the incidence of cancer of the pancreas, for males and females: Connecticut, 1935-1962.

SOURCE: Eisenberg, et al. (24).

These studies strengthen the earlier indications of an association between smoking and pancreatic cancer, but further research is needed in this area to elucidate the significance of this association.

## GENITO-URINARY CANCER

### CANCER OF THE BLADDER

As stated in the 1967 Report, there has been no increase in male or female death rates for cancer of the bladder over the 15 year period 1950-1964. However, the incidence rates for males have increased over 75 percent in the 25-year period from 1935-37 to 1960-62, and about 26 percent in the 15 year period from 1945-47 to 1960-62.

Deeley, et al. (16) reported on a retrospective study of 127 patients with cancer of the bladder and 126 patients with lung cancer, all matched with controls. The smoking "factors" (amount times duration of smoking) were significantly greater among cases than controls for both cancer sites. Even by age-groups, the "mean smoking factor" for either cancer was higher for cases than for controls. Preliminary data



FIGURE 5—Age-adjusted rates of the incidence of cancer of the bladder, for males and females: Connecticut, 1935-1962.

SOURCE: Eisenberg, et al. (24)

from a prospective study (37) in Japan shows a higher frequency of deaths from bladder cancer among smokers.

Certain amino acids, as found in tobacco, form trace amounts of alpha- and beta-naphthylamines upon pyrolysis (59). The latter agent is an established bladder carcinogen. So far, however, only its isomeric alpha-naphthylamines has been identified in cigarette smoke (60, 67).

Further investigation is needed on the carcinogenic metabolites of tryptophan which have been shown to be increased in the urine of cigarette smokers (92).

### CANCER OF THE KIDNEY

The 1967 Report did not mention the association between smoking and cancer of the kidney.

The U.S. Veterans study (46) shows increasing mortality ratios for cancer of the kidney with the amount of cigarette smoking. There is no apparent relationship with pipe and/or cigar smoking.

TABLE 3.—Mortality ratios and death rates for cancer of the kidney in U.S. veterans, by age, type and amount smoked for current smokers only

	Number of cigarettes smoked per day					Pipe and/or cigars	Cigars	Pipe
	0	1-9	10-20	21-39	40 and over			
Mortality ratios.....	1. 00	. 97	1. 34	1. 68	2. 75	1. 15	. 77	1. 32
Death rates:								
Age 45-54.....								
Age 55-64.....	8	5	8	10	26	5	7	2
Age 65-74.....	14	7	15	27	13	14	2	25
Age 75-84.....	7					40		

SOURCE: Kahn, H. A. (46).

TABLE 4.—Mortality ratios and death rates for cancer of the kidney in male cigarette smokers, by specified age groups

	Cigarette smokers	
	Age 45-64	Age 65-79
Mortality ratios.....	1. 42	1. 57
Death rates.....	<sup>1</sup> (4)6	<sup>1</sup> (15)23

<sup>1</sup> Numbers in parentheses indicate death rates for persons who have never smoked regularly.

SOURCE: Hammond, E. C. (34).

Hammond (34) has also demonstrated higher mortality ratios in cigarette smokers for cancer of the kidney.

Preliminary evidence from a retrospective study in progress (102) suggests that cigarette smokers, especially those who smoke over 35 cigarettes a day, are over-represented in those patients with cancer of the kidney. More research should be done to try to ascertain if there is a meaningful relationship between smoking and cancer of the kidney.

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