

Alcohol and Mortality

A Ten-Year Kaiser-Permanente Experience

ARTHUR L. KLATSKY, M.D.; GARY D. FRIEDMAN, M.D.; and ABRAHAM B. SIEGELAUB, M.S.;
Oakland, California

We studied 10-year mortality in relation to baseline alcohol use habits among four groups of 2015 persons, well matched for age, sex, race, and cigarette smoking. Persons reporting daily use of two drinks or fewer fared best; the heaviest drinkers (six or more drinks) had a doubled mortality rate, and users of three to five drinks had a mortality rate approximately 50% higher. The nondrinkers had a mortality rate similar to that of users of three to five drinks per day. Cancer, cirrhosis, accidents, and nonmalignant respiratory conditions contributed significantly to the excess mortality of the heavier drinkers; coronary disease mortality was significantly higher among nondrinkers. Smoking intensity was a possible factor in the increased mortality of heavier drinkers, but the data were also compatible with the hypothesis that smoking and drinking are synergistic in the production of certain cancers and nonmalignant chronic respiratory illness. Other traits associated with alcohol use or abstinence are possible contributors to the excess mortality of both heavy drinkers and nondrinkers.

THE DIRE CONSEQUENCES of chronic ingestion of large amounts of alcohol have been well documented in alcoholics, problem drinkers, or alcohol addicts (1-4). The approximate doubling of their mortality rate derives largely from deaths due to cirrhosis, accidents, infections, and, in some studies, certain malignancies and cardiovascular diseases. The few available population studies (5-9) also indicate a higher mortality rate among heavier drinkers, but these results have been less clear, perhaps due to the presence of relatively small numbers of heavier drinkers. At the other end of the drinking spectrum, abstainers from alcohol appear to fare worse with respect to mortality than persons who use small amounts of alcoholic beverages (6-9).

Drinking habits are strongly related to cigarette smoking (10, 11), and cigarette smoking is a powerful predictor of mortality from various causes (12, 13). Some of the earlier studies (1-3) were not controlled for smoking.

We have examined 10-year mortality rates among a large number of persons having various alcohol habits, in a study well controlled for smoking habits. The results show considerable disparity in the relation of various causes of death to alcohol consumption and further suggest that interactions with smoking affect the drinking-mortality association.

Methods

The study population was selected from 87 926 white or black men and women who had multiphasic health examina-

tions at either the Oakland or San Francisco Kaiser-Permanente facilities between July 1964 and August 1968. This number of examinees is equal to 48% of the 182 357 persons of all races who were Kaiser Foundation Health Plan members in these cities on 30 March 1968. The multiphasic procedure, which has been described elsewhere (14), contained a self-administered questionnaire that included these two questions about alcohol use: In the past year, did you drink any alcohol? If yes, how many alcoholic drinks did you usually have (wine, beer, whiskey, cocktails)? The options to be checked were nine or more a day, six to eight a day, three to five a day, or two or fewer a day. There were 19 895 nondrinkers (no to question 1), 51 481 persons who reported use of two or fewer drinks per day, 7074 who took three to five drinks per day, and 2084 who reported daily use of six or more drinks. The remainder (7392) failed to complete both questions satisfactorily.

We attempted to match by computer selection each of the 2084 persons reporting use of more than six drinks to each of three controls: a nondrinker, a person taking two or fewer drinks, and a person taking three to five drinks. All but 69 of those consuming six or more drinks were matched to each of three controls for sex, race, presence or absence of established cigarette smoking habit, examination date (within 24 months), and age (within 5 years). The 69 who could not thus be matched were excluded. More than 95% of the control subjects were matched within 1 year for age, and more than 50% were matched for examination date within six months. Matching was attempted for cigarette use intensity (one pack or less per day) and examination location (San Francisco or Oakland), but subjects were not discarded if these could not be matched. Thus, we selected four groups of 2015 persons each; the quality of the matching is shown in Table 1. Each group of 2015 persons included 1370 white men, 346 white women (total white = 1716), 214 black men, and 85 black women (total black = 299). Those who used six or more drinks daily included 1245 persons (mean age = 44.6 years) who reported daily use of six to eight drinks and 770 persons (mean age = 44.7 years) who reported use of nine or more drinks a day.

Mortality for all 8060 subjects was ascertained by search in California death indexes through 31 December 1976 for names of the 3190 subjects who were no longer listed as Kaiser Foundation Health Plan members on 30 June 1977. Matching names were confirmed by comparing health plan record information with death certificate data. In a previous study (13) we estimated, on the basis of U.S. mortality rates and the expectancy for this insured population of mortality rates lower than for the general population, that this method of mortality surveillance in California detected 82% to 92% of all deaths; the remainder represents mortality in other states. Causes of death were coded according to the International Classification of Diseases Adapted, eighth revision.

Total mortality and mortality by specific cause were computed for the alcohol use groups as a percentage of the original 2015 persons in each group. Statistical comparisons were made using the McNemar chi-square method for matched pairs.

The multiphasic questionnaire contained the following item on drinking habits before the year preceding the examination date: Before one year ago, at any time in the past were you a heavy alcohol drinker? Mortality was analyzed for drinkers of various amounts with certain nonmatched traits (past heavy

Alcohol-Benefit

* From the Department of Medicine, Kaiser-Permanente Medical Center, and the Department of Medical Methods Research, Kaiser-Permanente Medical Care Program; Oakland, California.

Table 1. Matched Traits for Alcohol Use Groups*

Trait	Usual Number of Drinks/Day			
	0	≤2	3-5	6+
Mean age, yrs	44.7	44.7	44.7	44.7
Mean examination date	7/21/66	7/22/66	7/25/66	8/10/66
Established smokers, %	65.2	65.2	65.2	65.2
< 1 pack/d	14.7	11.5	11.5	11.5
≥ 1 pack/d	50.5	53.7	53.7	53.7
Not established smokers, %	34.8	34.8	34.8	34.8
Location, %				
San Francisco	50.5	59.1	57.7	59.5
Oakland	49.5	40.9	42.3	40.5

* There were 2015 persons in each group; controls matched to those taking six or more drinks per day.

drinkers, smokers of two or more packs per day, former cigarette smokers, persons who never smoked). Statistical comparisons for these used the independent samples chi-squared test.

Results

OVERALL MORTALITY

Table 2 presents data showing mortality from all causes among the persons with various alcohol habits. The 745 subjects who died included 177 nondrinkers, 126 persons reporting daily use of two or fewer drinks, 187 persons reporting use of three to five drinks, and 255 persons reporting use of six or more drinks. Setting the two or fewer drinkers at 1.00 (standard), the mortality ratios were 1.40 for nondrinkers, 1.48 for three to five drinkers, and 2.02 for six plus drinkers.

Trends were similar among men and women. The relation of alcohol use to mortality was strongest among persons under 50 years of age at entry into the study and was relatively weak among persons over age 60. Although the average age of blacks was 5 years younger than whites (with, consequently, a lower mortality rate), alcohol use showed an apparently stronger relation to mortality among whites than among blacks. The relation of alcohol

use to mortality was slightly stronger among established smokers, but was present in nonsmokers, too. The relatively small mortality difference between established smokers and nonsmokers reflects, in part, greater average age of the nonsmokers.

CANCER MORTALITY

Table 3 presents cause-specific mortality incidence: Cancer deaths (28.9% of all deaths) were significantly more numerous among drinkers of six or more daily and slightly more numerous among three to five than two or fewer drinkers or nondrinkers. Oropharyngeal plus esophageal cancers, lung cancer, and metastatic cancers of unspecified primary site were the only subgroups significantly more numerous among the drinkers of six plus drinks daily. All 15 persons who died of oropharyngeal or esophageal cancer were either users at entry into the study of three or more drinks daily or were acknowledged past heavy drinkers. Of the 62 persons who died of lung cancer, 45 were either three plus drinkers or past heavy drinkers.

CARDIOVASCULAR MORTALITY

Cardiovascular disease was the most frequent cause of

Table 2. Ten-Year Mortality According to Alcohol Use

Matched Groups	Mean Entry Age*	Usual Number of Drinks/Day				All Groups	Statistically Significant Differences (p < 0.01)†
		0	≤2	3-5	6+		
	yrs	← % mortality →					
All subjects (n = 2015)	43.3-43.4	8.8	6.3	9.3	12.7	9.2	6+ vs all ≤2 vs all
Men (n = 1584)	45.3-45.4	9.9	6.9	10.0	14.3	10.3	6+ vs all ≤2 vs all
Women (n = 431)	42.2-43.3	4.4	3.7	6.5	6.5	5.3	None
Entry age							6+ vs 0, ≤2
< 50 yrs (n = 1289-1307)		3.3	1.7	4.1	6.0	3.8	≤2 vs all
50-59 yrs (n = 494-510)*		13.9	10.9	12.6	22.0	14.8	6+ vs all
60+ yrs (n = 211-216)*		29.2	23.2	33.2	31.0	29.2	None
White (n = 1716)	45.6-45.7	9.3	6.4	9.8	13.7	9.8	6+ vs all ≤2 vs all
Black (n = 299)	40.2-40.3	5.7	5.4	6.4	6.7	6.0	None
Established cigarette smokers (n = 1314)	43.4-43.5	9.5	6.3	9.4	13.5	9.7	6+ vs all ≤2 vs all
Not current established smokers (n = 701)‡	47.1-47.2	7.4	6.1	9.0	11.1	8.4	6+ vs ≤2

* Age matching was close, but slight variations exist among the various alcohol groups.

† Because multiple group comparisons were made, we chose a conservative indicator of statistical significance. Many other comparisons were significant at p < 0.05. Many of the comparisons in this table were significant at p < 0.001.

‡ Includes persons who never smoked, ex-smokers, and cigar and pipe smokers.

Table 3. Death By Cause* According to Alcohol Habit

Cause of Death†	Usual Number of Drinks/Day (n = 2015, Each Group)				Total for All Groups (n = 8060)	Statistically Significant Difference (p < 0.01)‡
	0	≤2	3-5	6+		
All malignant neoplasms, (140-209)	45 (2.2)	42 (2.1)	53 (2.6)	75 (3.7)	215 (2.7)	6+ vs 0, ≤2
Oral cavity and esophagus (140-150)	2 (0.1)	0 (0.0)	5 (0.2)	8 (0.4)	15 (0.2)	6+ vs ≤2
Stomach (151)	3 (0.2)	3 (0.2)	3 (0.2)	4 (0.2)	13 (0.2)	
Colon and rectum (153-154)	3 (0.2)	7 (0.4)	5 (0.3)	4 (0.2)	19 (0.2)	
Pancreas (157)	2 (0.1)	5 (0.3)	3 (0.2)	6 (0.3)	16 (0.2)	
Lung (162)	15 (0.7)	7 (0.4)	16 (0.8)	24 (1.2)	62 (0.8)	6+ vs ≤2
Breast (174)	4 (0.2)	1 (0.1)	3 (0.2)	3 (0.2)	11 (0.1)	
Genitourinary (180-189)	3 (0.2)	8 (0.4)	7 (0.4)	4 (0.2)	22 (0.3)	
Central nervous system (191-192)	2 (0.1)	3 (0.2)	3 (0.2)	4 (0.2)	12 (0.1)	
Lymphatic and hematopoietic (200-209)	7 (0.4)	7 (0.4)	3 (0.2)	7 (0.4)	24 (0.3)	
Primary site unspecified (196-199)	2 (0.1)	0 (0.0)	3 (0.2)	7 (0.4)	12 (0.1)	6+ vs ≤2
Other specified site	2 (0.1)	1 (0.1)	2 (0.1)	4 (0.2)	9 (0.1)	
All cardiovascular (390-458)	88 (4.4)	64 (3.2)	82 (4.1)	77 (3.8)	311 (3.9)	
All coronary disease (410-414)	66 (3.3)	40 (2.0)	47 (2.3)	55 (2.7)	208 (2.6)	0 vs ≤2
Acute myocardial infarction (410)	36 (1.8)	22 (1.1)	29 (1.4)	22 (1.1)	109 (1.4)	
Other coronary (411-414)	30 (1.5)	18 (0.9)	18 (0.9)	33 (1.6)	99 (1.2)	
Stroke (430-438)	10 (0.5)	15 (0.7)	16 (0.8)	9 (0.5)	50 (0.6)	
Other cardiovascular (390-409, 415-429, 439-458)	12 (0.6)	9 (0.4)	19 (1.1)	13 (0.6)	53 (0.7)	
Respiratory (460-519)	7 (0.4)	3 (0.2)	12 (0.6)	18 (0.9)	40 (0.5)	6+ vs ≤2
Cirrhosis (571)	5 (0.3)	0 (0.0)	12 (0.6)	33 (1.6)	50 (0.6)	6+ vs all 3-5 vs ≤2
Accidents (800-959; E800-999)	16 (0.8)	8 (0.4)	19 (0.9)	39 (1.9)	82 (1.0)	6+ vs 0, ≤2
Other causes	16 (0.8)	9 (0.4)	9 (0.4)	13 (0.6)	47 (0.6)	
Total deaths	177 (8.8)	126 (6.3)	187 (9.3)	255 (12.7)	745 (9.2)	6+ vs all ≤2 vs all

*In California, from time of entry into study (1965 to 1968; mean dates = July 1966 through 31 December 1976).

†Numbers in parentheses indicate code numbers of the International Classification of Diseases Adapted, 8th revision.

‡Other comparisons were significant at p ≤ 0.05. Because we made multiple group comparisons, we chose a conservative indicator of significance for this table.

death (41.7% of all deaths). The cardiovascular deaths were most numerous among nondrinkers and least numerous among two or fewer drinkers, a difference largely reflecting a significant excess coronary mortality among nondrinkers. Among all groups, 109 deaths were attributed to acute myocardial infarction; those who drank more than six or two or fewer daily had the lowest mortality from this cause. Nearly all other coronary deaths were attributed to chronic ischemic heart disease (International Classification of Diseases Adapted [ICDA] 412.9), which showed a U-shaped curve (from nondrinkers to six plus drinkers) and was most frequent among six plus drinkers.

OTHER CAUSES OF DEATH

Most respiratory deaths (27 of 40) were due to emphysema, a diagnosis significantly more frequent among consumers of three to five and of more than six drinks than drinkers of two or fewer. Cirrhosis deaths had the expected strong relation to substantial alcohol use.

Deaths due to accidents, poisonings, and violence accounted for 11.0% of all mortality (82 of 745); almost half these occurred among six plus drinkers. Overall, deaths in these categories followed a U-shaped curve, with some excess among nondrinkers and substantial excess among heavier drinkers. Twenty-eight of these deaths were considered suicides; 12 of these were in six plus drinkers. Eighteen deaths were caused by motor vehicle accidents; nine of these were those who took six or more drinks per day. The 47 deaths due to miscellaneous causes included various neurologic, gastrointestinal, renal, infectious, and endocrinologic conditions.

MORTALITY AMONG HEAVY (SIX PLUS) DRINKERS

Mortality was slightly, but not significantly, higher among the 770 persons who reported daily use of nine or more drinks daily compared to the 1245 persons who reported use of six to eight drinks (14.3% for nine or more; 11.7% for six to eight). The mortality difference

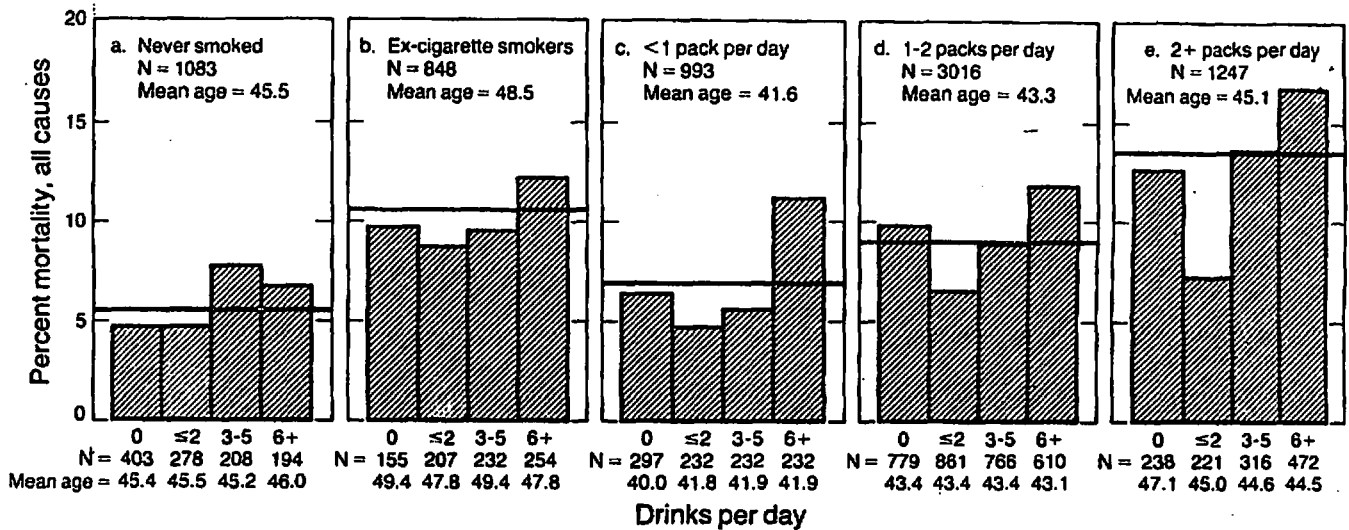


Figure 1. Percent mortality from all causes according to alcohol use and cigarette smoking history. The double horizontal bar represents the 10-year mortality for all persons with the indicated smoking history.

between those who took nine or more drinks and those who took six to eight was concentrated in the younger subjects; for those under age 50 at entry, this difference was significant (8.1% of nine or more and 4.7% of six to eight; $p < 0.05$).

Cardiovascular mortality was not higher among persons who took nine or more drinks than among those who took six to eight drinks (3.5% for nine or more; 4.0% for six to eight; not significant). For all noncardiovascular diagnoses combined, the mortality among nine plus drinkers was 10.8% and among drinkers of six to eight was 7.6% ($p < 0.05$). Mortality was slightly higher among nine or more than six to eight drinkers for each of the major causes of death except cardiovascular disease, including cirrhosis, accidents, nonmalignant respiratory disease, and cancer. The mortality rates for cancers of the lung, esophagus, and oropharynx were 1.9% for users of nine or more and 1.4% for users of six to eight drinks (not significant).

ANALYSIS BY SMOKING HABITS

Although the alcohol groups were well matched for established smoking and for use of one or more packs of cigarettes per day, further analysis showed a somewhat higher intensity of cigarette use among the heavier drinkers. The heavier drinkers included more persons who smoked two or more packs, more former smokers, a slightly larger fraction of persons who had smoked for over 20 years, and a slightly larger fraction of persons who inhaled when smoking. In contrast, the nondrinkers contained more persons who had never smoked, fewer ex-smokers, and fewer established smokers of one plus packs than any other group. Among nondrinkers who were established smokers or ex-smokers, there was no evidence of a higher intensity of cigarette use than among persons taking two or fewer drinks. Thus, smoking intensity might have contributed to the greater mortality of heavy drinkers but was unlikely to have been a factor in the excess mortality of nondrinkers compared to those taking two or fewer drinks.

Figure 1 presents data showing mortality (all causes)

according to drinking and cigarette habits. The 2084 persons (701 in each alcohol group) who were not established cigarette smokers included 1083 persons who had never smoked tobacco in any form (total mortality = 5.6%) and 848 nonsmokers who were ex-cigarette smokers (total mortality = 10.1%). The relatively high mortality of the ex-cigarette smokers (Figure 1) was explained substantially by the fact that the mean age of the ex-cigarette smokers was somewhat higher (48.6 years) than that of those who never smoked (45.3 years) or of established smokers (43.4 years). Among established smokers, mortality within each alcohol use category was clearly related to the number of cigarettes smoked (Figure 1), and the U-shaped alcohol-mortality curve is present at each smoking level.

In this study, all the major causes of death were associated with heavy smoking. Comparison of persons who smoked two or more packs to those who never smoked showed the following mortality ratios: cancer = 2.65; all cardiovascular disease = 1.76; coronary disease = 1.93; respiratory conditions = 3.50; cirrhosis = 3.50; accidents = 5.33.

The alcohol-cancer relation consisted predominantly of a higher mortality from cancers of the lung, esophagus, and oropharynx among persons who both drank and smoked heavily. Thus, 63% of persons who died of upper aerodigestive cancers had both a heavy drinking (three plus drinks per day or acknowledged past heavy drinking) and smoking (one plus packs daily) history. Further evidence for possible smoking-drinking interaction is seen at the extreme upper end of the smoking-drinking spectrum: Among smokers of two or more packs of cigarettes who took six to eight drinks, 1.9% (five of 264) died of these cancers; among smokers of two or more packs who took nine or more drinks, the upper aerodigestive cancer mortality was 4.3% (nine of 208).

A higher coronary mortality among nondrinkers compared to those taking two or fewer drinks was present in all smoking subgroups except those who never smoked. Among these persons, the coronary mortality was 1.5% of nondrinkers and 1.8% of two or fewer drinkers.

Table 4. Mortality According to Known Past Heavy Drinking

Mean Age, All (Range, Alcohol Groups)	yrs	Usual Number of Drinks/Day						All Groups
		0	≤2	3-5	6+	6-8	9+	
Past heavy drinkers*	45.6 (44.9-47.9)	12.9	9.6	11.0	14.5	13.3	16.1	13.2
Not past heavy drinkers	44.4 (44.1-44.6)	8.1	6.1	8.8†	10.7‡	10.1	11.9	8.1

* Those who answered yes to item about past heavy drinking included 286 (14.2%) nondrinkers, 115 (5.7%) persons using two or fewer drinks per day, 420 (21.3%) using three to five drinks per day, 623 (30.0%) using six to eight drinks per day, and 447 (58.0%) taking nine or more drinks per day.

† $p < 0.01$ versus ≤ 2 .
‡ $p < 0.001$ versus ≤ 2 .

ANALYSIS FOR PAST HEAVY DRINKING

Table 4 presents data showing that the mortality of acknowledged past heavy drinkers was higher at all drinking levels. Exclusion of the past heavy drinkers had little effect, however, on the U-shaped curve relating alcohol use and mortality. A high fraction of past heavy drinkers were established cigarette smokers; these persons were 2½ times more likely to smoke two or more packs than those who denied past heavy drinking (28.7% versus 11.4%). The excess mortality of past heavy drinkers is probably substantially related to associated smoking, as evidenced by the similarity of mortality rates of past heavy drinkers and those who had not been heavy drinkers among those who had never smoked (7.0% [seven of 100] and 5.5% [54 of 983], respectively).

Among the nondrinkers and two or fewer drinkers reporting past heavy drinking, coronary disease contributed substantially to the excess mortality: 5.5% of the nondrinkers and 4.4% of the two or fewer drinkers in these categories died of coronary disease (compared to 3.3% and 2.0% for all nondrinkers and two or fewer drinkers). However, removal of the past heavy drinkers did not eliminate a statistically significant difference in coronary mortality between these groups (3.0% of nondrinkers compared to 1.8% of two or fewer drinkers; $p < 0.05$).

Discussion

The Kaiser Foundation Health Plan membership is believed to represent a broad spectrum of the San Francisco Bay Area population, although the well-to-do and the indigent may be underrepresented. Persons with drinking problems may be underrepresented in this insured population, especially among those choosing to undergo a checkup. This study included, however, 96.7% of all examinees reporting daily intake of six plus drinks. The mortality outcome of this heaviest drinking group probably represents the causes of death among such drinkers in a general population. On the other hand, in order to better identify the effects of drinking per se, our control groups were matched to the heaviest drinking group and probably do not represent the general population. White men are overrepresented, and, especially among nondrinkers and persons reporting use of two or fewer drinks, the control groups contain a disproportionate number of established cigarette smokers.

We assume that some degree of underreporting of drinking habits occurred in our subjects, especially among those using substantial amounts of alcohol, and that any overreporting was minimal. Underreporting, by

including persons in drinking categories lower than those reflecting their true habits, tends to lessen apparent differences in mortality related to drinking. Nevertheless, we believe that this study, because of the large number of subjects and good control for smoking habits, provides many unique data.

The doubled mortality of those taking six or more drinks daily compared to that of the group representing the behavioral norm (two or fewer drinks) in our study population, is quite similar to the excess risk found in many of the studies (1-4) comparing "alcoholics" to the general population. Cirrhosis mortality contributed about one quarter of the excess deaths in six plus drinkers. The data are compatible with previous estimates (15) that 5% to 15% of heavy drinkers eventually die of cirrhosis. Violent deaths, with a well-known relation to substantial alcohol use, contributed another quarter of the excess mortality of six or more drinkers. The direct role of alcohol is difficult to separate from that of associated psychologic traits (16). The strong independent association of smoking to accidental and violent deaths suggests a major role of associated psychologic traits. Although the greater smoking intensity among heavier drinkers may be a factor in the excess of respiratory deaths, the data raise the question of an enhancing effect of alcohol. Heavy drinkers have long been thought to suffer more severe respiratory infections, and an independent deleterious effect of alcohol on pulmonary function has been suggested (17, 18) but not shown conclusively.

Our data confirm the strong epidemiologic evidence (19-25) linking alcohol use to oropharyngeal and esophageal cancer. Some (19, 25) have attributed an independent role to alcohol, but others (22, 24) believe that alcohol primarily enhances the role of tobacco. Nutritional (20, 24) and hygienic (20, 23) factors have been suggested.

The empiric relation of alcohol to lung cancer has been attributed to associated smoking (21, 25). We cannot rule out smoking intensity as a factor in the alcohol-lung cancer relation in our data, but we believe that the data are compatible with a hypothetical promoting or enhancing effect of alcohol in lung cancer production.

An indirect role for alcohol is suspected in liver cell cancer (20, 25), and reports have been presented linking alcohol to cancers of the colon and rectum (21), pancreas (26), prostate (1), and lymphatic-hematopoietic tissues (8). Opinion about these is divided; our data support none.

We found significantly more deaths due to cancer of

undetermined primary site among the users of six or more drinks daily (Table 3). This difference could represent delay in diagnosis or could mean that the heavier drinkers are more likely to have a highly malignant undifferentiated cancer. The question of cancer prognosis in relation to alcohol use warrants investigation.

We found only a slightly higher cardiovascular death rate among the heaviest drinkers than among the lightest drinkers. This result contrasts sharply with some previous studies (2-4, 27, 28) of problem drinkers that showed significantly higher cardiovascular mortality. Several of these studies were not controlled for smoking. Current evidence indicates disparate relations between alcohol and various cardiovascular diseases (29), including a positive association with hypertension (30), cardiomyopathy (29), and, possibly, stroke (18, 35) and an inverse relation to coronary disease (8, 31-34). Our data indicate infrequent death certificate diagnosis of hypertension or cardiomyopathy; the latter was diagnosed in three subjects, all users of three or more drinks per day. The relatively low incidence of fatal stroke may be due to the relative youth of our study groups.

The mortality data presented here show an alcohol-myocardial infarction relation generally similar to the findings in an earlier study among Kaiser Foundation Health Plan members of hospitalizations for infarction (31) and to hospitalization incidence for infarction in this study population (36). Both hospitalization studies showed the heaviest drinkers at least risk of acute infarction. The apparently greater mortality risk in this study of the heaviest (six plus) drinkers attributed to chronic ischemic heart disease presumably reflects syndromes other than infarction, such as congestive failure or sudden arrhythmia death. Such syndromes due to coronary disease may be more prevalent in heavy drinkers, but it has also been suggested (37, 38) that noncardiac death syndromes in such persons may commonly be assigned a coronary diagnosis. We therefore wonder about spurious cardiac diagnoses in this category. To this, we add a further speculation: that noncoronary but cardiac death actually due to alcohol (for example, cardiomyopathy or arrhythmia) may at times be misclassified as coronary disease.

Excess mortality among abstainers compared to drinkers of small amounts of alcoholic beverages has been found in several surveys (5-8) dating back to 1926 (5). Until recently, the excess death rate of nondrinkers was presumed to be attributable to various correlates of abstinence. However, this study and other recent reports (8, 31-34, 36) suggest that increased coronary events in abstainers are a major part of the explanation. Much interest exists in the high-density lipoprotein (HDL) cholesterol as a possible mechanism for a protective effect of alcohol because HDL cholesterol levels are inversely related to coronary events and directly related to alcohol use (32, 39). Curiously, tobacco tends to lower HDL cholesterol levels (40), so that alcohol and tobacco may counteract each other in this respect. A more immediate protective effect of alcohol has been proposed (41), perhaps an antiplatelet action (42).

Although abstinence from alcohol, especially in smokers, might result in increased coronary mortality, this possibility does not entirely account for the higher mortality risks of abstainers, and factors only indirectly related to current abstinence (for example, past drinking, psychologic traits) may account for the remainder of the increased risk. We have found that persons taking two or fewer drinks had, on average, a higher educational attainment than any other alcohol use group (11) and may therefore tend to have a healthier life style than persons of other alcohol use habits. It should also be noted that our lowest drinking category, two or fewer drinks per day, is a broad one; it includes persons who drink daily and those who drink only on special occasions. We do not know whether the favorable mortality experience applies equally to these subgroups.

The general public and individual patients wish guidelines about the benefits and risks of use of alcohol. We believe that it is easier for a health professional to counsel an individual patient than to form general rules. The hazards of chronic substantial drinking are obvious. The data presented here indicate that the threshold for increased mortality risk lies in the range of regular use of three to five drinks daily and that the risk rises sharply at six or more drinks per day. Is it safer to take small amounts of alcohol than to abstain entirely? The answer is clearly "no" for a person who may not be able to control his or her drinking. For most of the American adult population, which already uses no more than two drinks per day, the current evidence is reassuring.

ACKNOWLEDGMENT: The authors thank Gary Lee, who did the computer programming, and Morris Collen, M.D., Robert Feldman, M.D., Derek Crawford, M.D., Jacques Landy, Benjamin Klatsky, Cynthia Landy, May Kuwatani, and Della Mundy for assistance.

Grant support: in part by the Community Service Program of Kaiser Foundation Hospitals and by a grant from the U.S. Brewers' Association, Inc.

► Requests for reprints should be addressed to Arthur L. Klatsky, M.D.; Department of Medicine, Kaiser-Permanente Medical Center, 280 West MacArthur Boulevard; Oakland, CA 94611.

References

1. SUNDBY P. *Alcoholism and Mortality*. Oslo, Norway: Universitetsforlaget; 1967.
2. SCHMIDT W, DE LINDT J. Causes of death of alcoholics. *J Stud Alcohol*. 1972;33:171-85.
3. PELL S, D'ALONZO CA. A five-year mortality study of alcoholics. *J Occup Med*. 1973;15:120-5.
4. ROBINETTE CD, HRUBEC Z, FRAUMENI JF JR. Chronic alcoholism and subsequent mortality in World War II veterans. *Am J Epidemiol*. 1979;109:687-700.
5. PEARL R. *Alcohol and Longevity*. New York: Knopf; 1926.
6. SHURTLEFF D. Some characteristics related to the incidence of cardiovascular disease and death: Framingham Study, 16-year follow-up. In: KANNEL WB, GORDON T, eds. *The Framingham Study: An Epidemiological Examination of Cardiovascular Disease*. Section 26. Washington, D.C.: U.S. Government Printing Office; 1970.
7. UNITED STATES DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE. *Second Special Report to the Congress on Alcohol and Health from the Secretary of Health, Education, and Welfare*. Washington, D.C.: U.S. Government Printing Office; 1975. (DHEW publication no. [ADM] 75-212).
8. BLACKWELDER WC, YANO K, RHOADS GG, KAGAN A, GORDON T, PALESCH Y. Alcohol and mortality: the Honolulu heart study. *Am J Med*. 1980;68:164-9.
9. DYER AR, STAMLER J, PAUL O, et al. Alcohol consumption and 17-year mortality in the Chicago Western Electric Company Study. *Prev Med*. 1980;9:78-90.

10. CAHALAN D, CISIN IH, CROSSLEY HM. *American Drinking Practices*. New Haven: College and University Press; 1969.
11. KLATSKY AL, FRIEDMAN GD, SIEGELAUB AB, GERARD MJ. Alcohol consumption among white, black, or Oriental men and women: Kaiser-Permanente multiphasic health examination data. *Am J Epidemiol*. 1977;105:311-23.
12. UNITED STATES DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE, PUBLIC HEALTH SERVICE. Smoking and overall mortality. In: *The Health Consequences of Smoking: a Public Health Service Review: 1967*. Washington, D.C.: U.S. Government Printing Office; 1967:7-18. (PHS publication no. 1696).
13. FRIEDMAN GD, DALES LD, URY HK. Mortality in middle-aged smokers and nonsmokers. *N Engl J Med*. 1979;300:213-7.
14. COLLEN MF, DAVIS LF. The multitest laboratory in health care. *J Occup Med*. 1969;11:355-60.
15. BRODY JA, MILLS GS. On considering alcohol as a risk factor in specific diseases. *Am J Epidemiol*. 1978;107:462-6.
16. SCHMIDT W, POPHAM RE. Heavy alcohol consumption and physical health problems: a review of the epidemiological evidence. *Drug Alcohol Depend*. 1975;1:27-50.
17. EMIRGIL C, SOBOL BJ, HEYMANN B, SHIBUTANI K. Pulmonary function in alcoholics. *Am J Med*. 1974;57:69-77.
18. HEINEMANN HO. Alcohol and the lung: a brief review. *Am J Med*. 1977;63:81-5.
19. ROTHMAN K, KELLER A. The effect of joint exposure to alcohol and tobacco on risk of cancer of the mouth and pharynx. *J Chron Dis*. 1972;25:711-6.
20. KISSIN B, KALEY MM. Alcoholism and cancer. In: KISSIN B, BEGLEITER H, eds. *The Biology of Alcoholism*. Vol. 3. New York: Plenum Press; 1974:481-512.
21. WILLIAMS RR, HORM JW. Association of cancer sites with tobacco and alcohol consumption and socioeconomic status of patients: interview study from the Third National Cancer Survey. *J Natl Cancer Inst*. 1977;58:525-47.
22. WYNDER EL, MUSHINSKI MH, SPIVAK JC. Tobacco and alcohol consumption in relation to the development of multiple primary cancers. *Cancer*. 1977;40(suppl):1872-8.
23. GRAHAM S, DAYAL H, ROHRER T, et al. Dentition, diet, tobacco, and alcohol in the epidemiology of oral cancer. *J Natl Cancer Inst*. 1977;59:1611-8.
24. MCCOY GD, WYNDER EL. Etiological and preventive implications in alcohol carcinogenesis. *Cancer Res*. 1979;39:2844-50.
25. TUYNS AJ. Epidemiology of alcohol and cancer. *Cancer Res*. 1979;39:2840-3.
26. BURCH GE, ANSARI A. Chronic alcoholism and carcinoma of the pancreas: a correlative hypothesis. *Arch Intern Med*. 1968;122:273-5.
27. WILHELMSEN L, WEDEL H, TIBBLIN G. Multivariate analysis of risk factors for coronary heart disease. *Circulation*. 1973;48:950-8.
28. DYER AR, STAMLER J, PAUL O, et al. Alcohol consumption, cardiovascular risk factors, and mortality in two Chicago epidemiologic studies. *Circulation*. 1977;56:1067-74.
29. KLATSKY AL. Effects of alcohol on the cardiovascular system. In: GASTINEAU CF, DARBY WJ, TURNER TB, eds. *Fermented Food Beverages in Nutrition*. New York: Academic Press; 1977:317-40.
30. KLATSKY AL, FRIEDMAN GD, SIEGELAUB AB, GERARD MJ. Alcohol consumption and blood pressure: Kaiser-Permanente multiphasic health examination data. *N Engl J Med*. 1977;296:1194-200.
31. KLATSKY AL, FRIEDMAN GD, SIEGELAUB AB. Alcohol consumption before myocardial infarction: results from the Kaiser-Permanente study of myocardial infarction. *Ann Intern Med*. 1974;81:294-301.
32. YANO K, RHOADS GG, KAGAN A. Coffee, alcohol and risk of coronary heart disease among Japanese men living in Hawaii. *N Engl J Med*. 1977;297:405-9.
33. HENNEKENS CH, WILLETT W, ROSNER B, COLE DS, MAYRENT SL. Effects of beer, wine, and liquor in coronary deaths. *JAMA*. 1979;242:1973-4.
34. BARBORIAK JJ, RIMM AA, ANDERSON AJ, SCHMIDHOFFER M, TRISTANI FE. Coronary artery occlusion and alcohol intake. *Br Heart J*. 1977;39:289-93.
35. KATSUKI S. Hisayama study. *Jap J Med*. 1971;10:167-75.
36. KLATSKY AL, FRIEDMAN GD, SIEGELAUB AB. Alcohol use and cardiovascular hospitalizations. *Circulation*. 1979;60(Suppl II):II-51. Abstract.
37. KULLER LH, PERPER JA, COOPER M, FISHER R. An epidemic of deaths attributed to fatty liver in Baltimore. *Prev Med*. 1974;3:61-79.
38. RANDALL B. Sudden death and hepatic fatty metamorphosis: a North Carolina survey. *JAMA*. 1980;243:1723-5.
39. CASTELLI WP, DOYLE JT, GORDON T, et al. Alcohol and blood lipids: the cooperative lipoprotein phenotyping study. *Lancet*. 1977;2:153-5.
40. CRIQUI MH, WALLACE RB, HEISS G, KISHKEL MA, SCHONFELD G, JONES G. Cigarette smoking and high density lipoprotein cholesterol—the lipid research clinics prevalence study. *CVD Epidemiol Newsletter*. 1980;28:26. Abstract.
41. HARTZ AJ, ANDERSON AJ, BARBORIAK PN, BARBORIAK JJ, HOFFMANN RG. Risk factors for myocardial infarction independent of coronary artery disease. *Circulation*. 1979;60(Suppl II):II-68. Abstract.
42. HAUT MJ, COWAN DH. The effect of ethanol II on hemostatic properties of human blood platelets. *Am J Med*. 1974;56:22-33.