Fourth Special Report to the U.S. Congress on

Alcohol and Health

from the Secretary of Health and Human Services

January 1981

U.S. Department of Health and Human Services
Public Health Service
Alcohol, Drug Abuse, and Mental Health Administration

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Men of all three races who took two or fewer drinks daily had mean blood pressures similar to those of nondrinkers. Women of all three races who took two or fewer drinks daily had blood pressures slightly lower than nondrinkers. Men and women of all races who took three or more drinks daily had higher systolic and diastolic blood pressure than either nondrinkers or persons who took two or fewer drinks daily. This relationship proved to be independent of smoking, coffee use, salt use, blood group, educational attainment, and adiposity. The blood pressure-drinking relationship was progressive up to six or eight drinks a day in whites and Orientals, and up to three to five drinks a day in blacks. Drinking beyond those levels caused no further increase in blood pressure.

The difference in mean blood pressure in the Kaiser-Permanente study translated into 100 percent higher prevalence of hypertension (defined as blood pressure of 160/95 mm Hg or higher) in white men and women who took six or more drinks daily compared with nondrinkers or users of two or fewer drinks daily. Among black men and women, the prevalence of hypertension among users of three or more drinks daily was increased by about 50 percent. The doubled prevalence among the white heavier drinkers was quite similar to the findings in other studies (Conway 1968; Kannell and Sorlie 1974) in which the methods of classifying data allowed comparison.

Although the agreement among various studies establishes an association between alcohol use and blood pressure, the possibility still exists that the association, at least in part, could be influenced by such factors as (1) psychosocial stress as an underlying factor for both hypertension and use of large amounts of alcohol; (2) a common hereditary predilection for both alcohol use and hypertension; (3) other environmental factors such as dietary habits; or (4) alcohol withdrawal, which is associated with increased heart rate and blood pressure in some heavy drinkers (Wallace 1980).

A physiologic mechanism has not been established for the association between alcohol consumption and blood pressure elevations, though there has been some speculation that chronic corticosteroid excess (Rees et al. 1977; Smals and Kloppenborg 1977), or action through the renin-angiotensin hormone system (Linkola 1979) may be involved.

The possibility of true direct association between alcohol consumption and blood pressure is strong enough to lead some health practitioners to advise hypertensive patients who take three or more drinks a day (35 ml or more of absolute alcohol) to cut down (Klatsky in press).

Alcohol and Coronary Atherosclerosis

In the first half of this century there were a number of reports of an apparent inverse relation between chronic substantial alcohol use and atherosclerotic disease, including coronary disease. However, this was dismissed by some investigators (Parrish and Eberly 1961; Ruebner et al. 1961) as probably due to the tendency of alcoholics to die young, before they develop atherosclerosis. Some later reports (Chapman et al. 1974; Paul et al. 1963) also showed no association between alcohol use and coronary events.

There is little epidemiologic evidence to suggest that a relationship exists between alcohol and atherosclerosis in the aorta and peripheral vessels (Klatsky 1980; Klatsky et al. 1979*a*).

More recent studies have reported an inverse relationship (drinkers at less risk) between alcohol use and heart attacks (myocardial infarction) (Blackwelder et al. 1980; Friedman et al. 1974; Hennekens et al. 1978, 1979; Klatsky 1980; Klatsky et al. 1974, 1976; Kozarevic et al. 1980; Stason et al. 1976; U.S. National Heart Institute 1966; Yano et al. 1977). Although the relationship was not statistically significant and other risk factors were not controlled in some of the earlier studies, statistical significance, as well as control for smoking and other risk factors, has been achieved in several studies. In the Kaiser-Permanente studies (Friedman et al. 1974; Klatsky et al. 1974, 1976, 1979*b*), the largest difference in coronary risk was the difference between current nondrinkers (including past drinkers) and light to moderate drinkers (two or fewer drinks per day), but the inverse drinking-coronary relationship was slightly progressive up to six or more drinks daily. There was no significant relationship, positive or negative, between reported past heavy drinking and heart attack.

A recent study by the Kaiser-Permanente Program (Klatsky 1980; Klatsky et al. 1979*a*) showed a significantly lower hospitalization incidence for coronary disease among drinkers than among nondrinkers. These data were derived from followup of four matched groups of 2,105 persons each, including nondrinkers and users of two or fewer, three to five, and six or more drinks per day. Among these 8,060 persons there was again a slightly progressive inverse relationship between drinking up to six or more drinks per day and heart attack, but as in the earlier Kaiser-Permanente study, the largest difference in heart attack risk was between nondrinkers and those who had two or fewer drinks daily.

While most of the population studies suggest that drinkers suffer fewer major coronary events, studies of problem drinkers and alcoholics show the opposite. These include reports from studies of duPont employees (D'Alonzo and Pell 1968), the State of California Alcoholic Rehabilitation Program (California State Department of Public Health 1961), alcoholics in a rehabilitation program in Toronto (Schmidt and deLint 1972), Swedish Temperance Board registrants (Wilhelmsen et al. 1973), problem drinkers in the Chicago Peoples Gas Company in Chicago (Dyer et al. 1977), and heavy drinkers (five or more drinks a day) among Western Electric Company employees in Chicago (Dyer et al. 1977).

Caution in interpreting the reports on the presumably beneficial effects of moderate alcohol is clearly warranted. Based on present information, encouraging the use of alcohol to reduce the likelihood of occurrence or recurrence of heart disease must be questioned because it has been noted that any potential benefits to be derived appear to be outweighed by the attendant risks associated with increasing alcohol consumption (Blackwelder et al. 1980; Castelli et al. 1977; Knochel et al. 1975; Kozarevič et al. 1980). These risks include adverse effects on the cardiovascular system such as hypertension, stroke, and alcoholic cardiomyopathy, as well as other health and social hazards cited elsewhere in this report.

The High-Density Lipoprotein-Cholesterol Hypothesis

A plausible mechanism for a protective effect of small amounts of alcohol in coronary disease is based on the observation that alcohol raises high-density lipoprotein cholesterol (HDL-C) levels in blood (Bradley et al. 1978; Castelli et al. 1977; Danielsson et al. 1978; Garrison et al. 1978; Grande et al. 1960; Hartung et al. 1980; Hulley 1980; Hulley et al. 1977; Johansson and Laurell 1969; Johansson and Medhus 1974; Kuller 1980; Rhoads, Kagan, and Yano 1976; Wallerstedt et al. 1977). Other studies have shown that elevated HDL-C is inversely related to coronary atherosclerotic disease and may play a protective role by aiding in removal of cholesterol from the body by retarding the formation of atherosclerotic plaques (Castelli 1980; Goldbourt and Medalie 1977; Rhoads, Gulbrandsen, and Kagan 1976). The effect of alcohol in raising HDL levels is generally proportional to the amount regularly taken (Hulley 1980). Alcohol-induced HDL-C elevations decrease in days to weeks when drinking is stopped (Hulley 1980; Kuller 1980). There is evidence that the site of action of alcohol's influence on HDL is in the liver; in some very heavy drinkers with acute or severe liver disease the HDL levels may be very low, presumably as a consequence of hepatic injury, which limits the liver's capacity to synthesize or secrete lipids and lipoproteins (Kuller 1980; Sabesin in press).

Thus evidence exists that high HDL-C protects against the development of coronary heart disease, and that alcohol appears to elevate HDL-C when taken in quantities that do not damage the liver. It is tempting to speculate cause and effect from these data; that is, that alcohol use increases HDL-C, which in turn decreases coronary occlusion. However, while evidence that alcohol and HDL are linked is mounting, the hypothesis that this link means that alcohol protects against coronary disease is not yet firmly established.

These possibly beneficial effects of moderate alcohol on HDL-C must be separated from the deleterious effects of excessive alcohol use on the liver and its secondary effects on lipoprotein metabolism (Baraona and Lieber 1979; Sabesin et al. 1979, 1980; Sabesin, Hawkins, Kuiken, and Ragland 1977; Seidel et al. 1972; Ragland, Bertram, and Sabesin 1978). Alcohol use leading to alcoholic hepatitis actually causes abnormal HDL metabolism and very low levels of HDL-C (Freeman et al. 1977; Ragland, Heppner, and Sabesin 1978; Sabesin, Hawkins, Kuiken, and Ragland 1977; Sabesin et al. 1979, 1980). With the development of alcohol cirrhosis, and eventually liver failure, persistent derangements in hepatic cholesterol and triglyceride synthesis and in plasma lipoprotein metabolism occur (Sabesin in press). Since HDL-C is decreased in alcoholic liver disease, it might seem contradictory that some individuals dying from alcoholism and alcoholic cirrhosis have less evidence of coronary heart disease and atherosIcerosis. The explanation may reside in the fact that the profound abnormalities in lipoprotein metabolism and the low HDL-C associated with alcoholic liver disease may occur for relatively brief periods in the life of an alcoholic, whereas sometimes it is decades before alcohol significantly damages the liver. Sabesin (in press) has suggested that during those decades alcohol may exert effects on hepatic and lipoprotein metabolism that lead to high HDL-C concentrations in blood and consequently afford some protection against coronary heart disease.

Alcohol and Other Cardiovascular Disease

A positive relation between drinking and stroke incidence has been reported (Blackwelder et al. 1980; Castelli 1980; Kagan 1980; Katsuki 1971; Klatsky 1980; Klatsky et al. 1979*a*). The relationship is stronger for hemorrhagic than for thrombotic stroke (Blackwelder et al. 1980; Klatsky et al. 1979*a*) and is felt to be not entirely explained by the association of both drinking and stroke with hypertension. A bleeding tendency due to alcohol has been implicated as a possible additional explanation (Kagan 1980).

An unusual form of angina pectoris, known as Prinzmetal variant angina, is widely believed to be related in some patients to reversible spasm of large coronary vessels (Rosenblatt and Selzer 1977). Although alcohol has been reported to be one of the pharmacologic agents that can induce the phenomenon (Fernandez et al. 1973), the association has not been widely observed. A number of cases of myocardial infarction have been reported among alcoholics with no evidence of atherosclerosis or thrombotic occlusion (Regan et al. 1975), and a mechanism of external constriction of coronary vessels by scarring due to alcoholic cardiomyopathy was postulated. Myocardial infarction without atherosclerosis is a poorly understood event that also occurs occasionally in nonalcoholics (Rosenblatt and Selzer 1977).

Substantial alcohol use has been reported to be associated with a higher incidence of venous conditions, such as phlebitis and varicose veins (Klatsky 1980).

Alcohol and the Endocrine System

The effects of alcohol on several endocrine systems were reviewed in the *Third Special Report on Alcohol and Health* (U.S. Department of Health, Education, and Welfare 1978). Currently, much research interest is focused on the effects of alcohol on the metabolism of testosterone (male hormone), perhaps because the systems involved in the synthesis and degradation of that hormone are easier to work with.

Effects of Alcohol on Male Hormone Levels

Numerous studies have shown that acutely or chronically administered alcohol lowers serum testosterone levels in males of all species, including man (Badr and Bartke 1974; Baker et al. 1976; Cicero and Badger 1977; Cicero, Bell, and Badger 1980; Cicero, Bell, Meyer, and Badger 1980; Cicero, Bernstein, and Badger 1978; Cicero, Meyer, and Bell 1978; Distiller et al. 1976; Dotson et al. 1975; Farmer and Fabre 1975; Gordon and Southren 1977; Gordon et al. 1976, 1978; Lester and Van Thiel 1977; Marks and Wright 1977; Mendelson and Mello 1974; Mendelson, Ellingboe, Mello, and Kuehnle 1978; Mendelson, Mello, and Ellingboe 1978; Mendelson et al. 1977; Persky et al. 1977; Southren and Gordon 1970, 1976; Symons and Marks 1975;